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# (54) Production and purification of cathepsin L for X-ray crystallography

(57) Cathepsin L is a thiol protease and produced by cloning human epithelial cell DNA into E. coli using a secretion vector. The proenzyme is secreted into the periplasmic space of the E. coli and purified to a high specific activity (at least 40.000 nmoles/min/mg). The purified, correctly folded enzyme was crystallised and X-ray coordinates determined for use in rational drug design.



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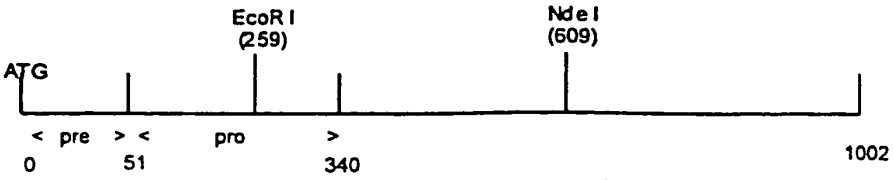
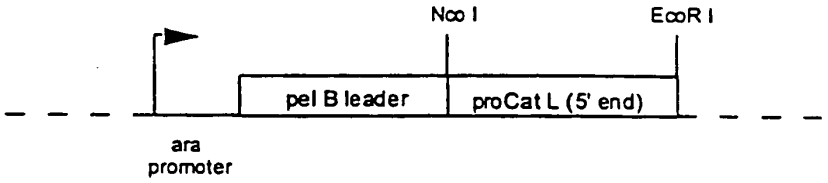
# Figure 1

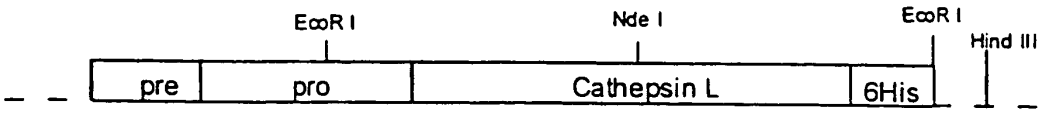



preproCathepsin L

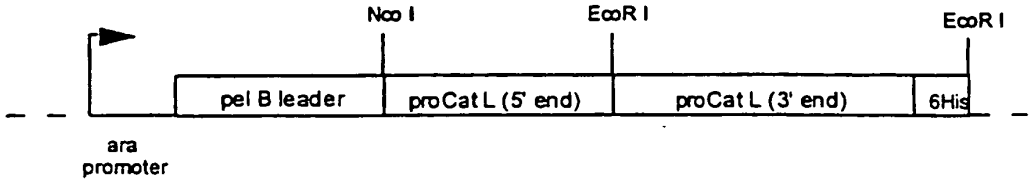
# Figure 2




# Figure 3



# Figure 4




pDP 483

2306961

# PROTEIN

The present invention relates to cathepsin L in biologically active form, methods of making cathepsin L in *E. coli*, cathepsin L in crystalline form, use of the X-ray structure atomic co-ordinates in rational drug design and drugs obtained thereby.

Cathepsin L is a thiol protease that plays an important role in the degradation of proteins within the lysosomes and in the extracellular matrix. It occurs in at least three forms: prepro-; pro- and; mature cathepsin L. Furthermore, mature cathepsin L can be "clipped" through proteolysis to yield heavy and light chains. The pro and prepro forms are biologically inactive.

Besides its role in protein turnover, cathepsin L has been implicated in bone remodelling, glomerulonephritis, rheumatoid arthritis, antigen processing and tumour metastasis. The search for drugs that intervene in these diseases has been impeded by lack of knowledge as to the three-dimensional structural determinants of the specificity of cathepsin L. These can only be accurately ascertained through the technique of X-ray crystallography, which involves the analysis of X-ray diffraction of a crystalline sample.

Obtaining a crystalline sample suitable for the structural analysis of cathepsin L has eluded all researchers to date. The supply of pure active protein for crystallisation trials has been a major stumbling block in the growth of large crystals. Whilst not wishing to be bound by theoretical considerations the presence of a free cysteine residue at the active site (which can cause mis-matched disulphide bond pairing) probably contributes to making the folding process complex. The sensitivity of the enzyme to extremes of pH also makes the enzyme difficult to handle because it is often desirable to work with the enzyme at extremes of pH such as for example in refolding experiments.

Abbreviations:

| | |
|---|---|
| CM | carboxymethyl |
| dOT | dissolved oxygen tension |
| NHMec | 7-amido-4-methyl-coumarin |
| MPD | methylpentandiol |
| NTA | nitrilo-triacetic acid |
| OTR | oxygen transfer rate |

| | |
|---|---|
| OUR | oxygen uptake rate |
| PAGE | polyacrylamide gel electrophoresis |
| PCR | polymerase chain reaction |
| SDS | sodium dodecyl sulphate |
| VVM | volume volume per minute |
| Z | benzyloxycarbonyl |

In an early report Smith and Gottesman (1989) in J. Biol. Chem. 264, 20487-20495, described the expression of human procathepsin L in *E. coli* as an insoluble product in inclusion bodies. They described the isolation and subsequent solubilisation of inclusion bodies followed by folding then activation (by acid treatment) of the enzyme to produce active enzyme in poor yield (<1% by activity). The authors reported that the majority of the product in the renaturation extract was insoluble and by implication misfolded. After purification by Sephadex G-75 chromatography the specific activity (as measured by the Z-Phe-Arg-NHMec assay described below) of the purified folded product was low (22,000 nmol/min/mg) implying that only a portion of the final pure product was in the correctly folded state.

Dolinar et al ( (1995) Biol. Chem. Hoppe-Seyler, 376: 385-388 ) have also described the expression of procathepsin L in *E. coli* as an insoluble product in inclusion bodies, followed by extraction and solubilisation of the inclusion bodies then folding of procathepsin L followed by acid activation. Despite improvements in yield to 4.4%, the authors calculate that only 30% of their folded cathepsin L product is active, implying that 70% of the product is inactive, presumably still misfolded. The misfolded enzyme would act to frustrate the crystallisation of the enzyme as the misfolded enzyme would interfere with the build up of ordered arrays of molecules that constitute the formation of the crystal.

The present invention is based on overcoming several technical hurdles: (1) we have secreted procathepsin L into *E. coli* periplasm in soluble form; (2) we have purified active cathepsin L from the growth medium in milligram amounts at high specific activity >100,000 nmoles/min/mg; (3) we have devised a process for the production of correctly folded molecules from soluble incorrectly folded molecules; (4) we have obtained cathepsin L in a crystalline form; (5) collected an X-ray diffraction data set from the crystals and; (6) we have determined the 3-dimensional structure of cathepsin L from the

X-ray diffraction data. This involved using papain as a model in molecular replacement procedures. The structure has been refined to give an accurate model which is used to understand the enzyme specificity and forms the basis of rational drug design.

According to one aspect of the present invention there is provided protein cathepsin L in which at least 40 % of the protein is correctly folded in a biologically active conformation. Preferably at least 50 % of the protein is correctly folded, more preferably at least 60 % of the protein is correctly folded, more preferably at least 70 % of the protein is correctly folded, more preferably at least 80 % of the protein is correctly folded, more preferably at least 90 % of the protein is correctly folded and especially at least 95 % of the protein is correctly folded.

The term "cathepsin L" as used herein (unless otherwise apparent from the context used) includes analogues or variants such as for example cathepsin L - $(His)_6$ where the $(His)_6$ tag is used to assist purification but other analogues are contemplated especially conservative analogues which would not unduly alter the biological properties of the protein. Generally cathepsin L is in isolated form meaning it is at least partially purified from its naturally occuring state.

The terms "Cathepsin L-6His" and "cathepsin L - $(His)_6$" refer to cathepsin L with a tag of 6 histidine amino acids added to its C-terminus.

According to another aspect of the present invention there is provided cathepsin L at a specific activity of at least 40,000 nmoles/min/mg. Specific activity is determined using the Z-Phe-Arg-NHMec assay described below. Preferably the specific activity is at least 50,000 nmoles/min/mg, more preferably the specific activity is at least 60,000 nmoles/min/mg, more preferably the specific activity is at least 70,000 nmoles/min/mg, more preferably the specific activity is at least 80,000 nmoles/min/mg, more preferably thespecific activity is at least 90,000 nmoles/min/mg and especially the specific activity is at least 100,000 nmoles/min/mg.

According to another aspect of the present invention there is provided a method of making cathepsin L which comprises directed expression of procathepsin L encoded on an expression vector into the periplasm of *E.coli* cultured in a growth medium. Preferably the E.coli is cultured at a temperature of 15-30°C and especially at 25°C. Preferably the expression vector comprises inducible expression control and the growth medium

comprises a concentration of inducer optimised for maximal soluble expression of cathepsin (this is a lower concentration, optimised for example by titration, than the concentration of inducer required for maximal expression of cathepsin). Culture of E.coli at low temperature (15-30°C ) gives a slow rate of cathepsin production which has the advantage of producing higher yields of correctly folded soluble cathepsin; use of a low concentration of inducer enhances this advantageous effect. Preferably soluble cathepsin L is collected from growth medium and activated by removal of the pro sequence and clipping the cathepsin into its 2-chain form..

According to another aspect of the present invention there is provided a secretion vector for directed expression of cathepsin L into the periplasm of *E.coli*.

According to another aspect of the present invention there is provided an *E.coli* host comprising a secretion vector for directed expression of procathepsin L into the host periplasm.

According to another aspect of the present invention there is provided *E. coli* MSD 2148 (MSD 213 pZen 1677) deposited under the Budapest Treaty as NCIMB accession no 40773 on 11th October 1995 with the National Collection of Industrial & Marine Bacteria, 23 St Machar Drive, Aberdeen AB2 1RY, Scotland, United Kingdom.

According to another aspect of the present invention there is provided cathepsin L in crystalline form. Preferably the crystals possess a monoclinic space group $P2_1$, with unit cell dimensions $a = 46.23$, $b = 49.38$, $c = 49.25$ Å and $\beta = 113.45°$. Preferably the crystals are wedge-shaped crystals and are preferably about 0.1 $mm^3$. Preferably the crystals essentially have the atomic coordinates set out in Example 4.

According to another aspect of the present invention there is provided X-ray coordinates of cathepsin L. Preferably the coordinates are substantially as set out in Example 4. Preferred X-ray coordinates are of the active site of cathepsin L as defined in Example 4 in residues 17-26, 29, 61-75, 111-118, 132-145, 158-166, 183-189 & 209-214.

According to another aspect of the present invention there is provided the use of the 3-dimensional structure of cathepsin L as determined from X-ray diffraction data in rational drug design. Preferred methods are described in Example 3 such as any of the following:

searching real and virtual compound databases for potential drugs; computational growth of ligands in the active site; and collecting X-ray diffraction data from crystals comprising potential drug.

According to another aspect of the present invention there is provided a novel inhibitor of cathepsin L determined by rational drug design using X-ray diffraction data of cathepsin L. The cathepsin L catalytic residues, ie those who play an active role in catalysis,

are Cys25, His163, Gln19, Asn183, and, in a structural role, Trp185. This however, is a configuration conserved in almost all cysteine proteases, and we need to look beyond the active site when carrying out drug design specific to cathepsin L. In fact, the surface of the entire active site cleft can be important. The following residue ranges form the active site cleft and therefore are most likely to be involved in drug design: 17-26, 29, 61-75, 111-118, 132-145, 158-166, 183-189, 209-214. Note that any one drug would only interact with a subset of these.

The invention will now be illustrated by the following non-limiting examples in which:

SEQ ID NO: 7 illustrates a cDNA nucleotide sequence of cathepsin L in which 289-339 represents signal peptide, 289-1290 represents pro-cathepsin L and, 340-1290 represents mature cathepsin L (Gal S. 1988, Biochem. J. 253, 303-306);

SEQ ID NO: 8 illustrates an amino acid sequence of cathepsin L in which 1-17 represents signal peptide, 18-113 represents pro peptide, 114-288 represents heavy chain and 292-333 represents light chain (Ritonja 1988, FEBS Letters 228, 341-345; Mason 1986, Biochem. J. 240, 373-377; Joseph 1987, Nucleic Acids Research 15, 3186) and;

Figure 1 illustrates a cloned PCR product showing restriction sites;

Figure 2 illustrates pDP480;

Figure 3 illustrates pCRII/cathepsin L-6-His and;

Figure 4 illustrates pDP483 (pZEN1677).

**Example 1 - Producti n of recombinant human cathepsin L-6His**

**1.1 Cloning of Cathepsin L-6His**

The coding sequence for full length preprocathepsin L was generated from a human epithelial cell cDNA library by PCR using oligonucleotides complementary to the 5' and 3' ends:

5' - 3' Oligonucleotide:

GCAGTAAGATATGAATCCTACACT (SEQ ID NO: 1)

3' -5' Oligonucleotide: (listed 5' - 3')

CATCACCGTCCACAGCTCACACAG (SEQ ID NO: 2)

The PCR product generated was cloned into the PCR cloning vector pCR II (InVitrogen). A diagram of the cloned PCR product showing relevant restriction sites is shown in Figure 1. This construct formed the starting material for generation of the *E.coli* secretion vector construct.

**1.2 Generation of *E.coli* procathepsin L-6His secretion vector**

The vector used for secretion of Cathepsin L in *E.coli* was **pAG170.** In pAG170, sequences to be expressed are cloned downstream of the *Erwinia carotovora* pel B secretory leader sequence under control of the ara B/C promoter from *Salmonella typhimurium*.

For cloning into pAG170, a PCR product was generated incorporating the sequence from the start of the pro region to the internal EcoR I site of procathepsin L, using the initial Cathepsin L construct above as the target DNA . The 5'-3' oligonucleotide also introduced a Nco I restriction site. The 3'-5' oligonucleotide was complementary to sequence encompassing the internal EcoR I site.

5'-3'oligonucleotide:

Nco I

GATGACCATGGCGACTCTAACATTTGATCACAG (SEQ ID NO: 3)

3'-5' oligonucleotide:

EcoR I

CTGCCTGAATTCTTCACTGGTCATGTCTC (SEQ ID NO: 4)

The PCR product generated was digested with Nco I and EcoR I and cloned into Nco I / EcoR I digested pAG170. A clone with correct sequence was identified (as pDP 480) and is shown diagramatically in Figure 2. The 3' end of procathepsin L from an internal Nde I site to the end of the coding sequence was then generated by PCR. The 5' - 3' oligonucleotide encompassed the internal Nde I site . The 3' - 5' oligonucleotide was designed so as to introduce a 6 histidine residues (for purification purposes) immediately upstream of the translational stop codon as well as EcoR I and Hind III restriction sites downstream of the coding sequence.

5' - 3' Oligonucleotide:

Nde I

CTATCCATATGAGGCAACAGAAGAATCCTG (SEQ ID NO: 5)

3' - 5' Oligonucleotide:

Hind III EcoR I stop codons 6 His tag

GACAAGCTT GAATTC TTA TTA GTGATGGTGATGGTGGTG

CACAGTGGGGTAGCTGGCTG (SEQ ID NO: 6)

The PCR product obtained was digested with Nde I and Hind III and cloned back into Nde I / Hind III digested pCR II preprocathepsin L to replace original sequence. The sequence of the 6-His tagged 3' Nde I - EcoRI fragment was confirmed (including sequence upstream of the Nde I site). A diagram of pCRII/Cathepsin L-6His is shown in Figure 3.

To complete the cloning of procathepsin L into the secretion vector, the fragment of procathepsin L-6His from the internal EcoR I site to the EcoR I site at the 3' end was excised from the pCR II construct and cloned into EcoR I digested pDP480. A clone of the correct orientation was identified. This generates a tetracycline resistant plasmid encoding procathepsin L-6His downstream of an in-frame pel B secretion leader, whose expression is under the control of an ara B/C promoter / regulator cassette.This construct was initially

designated pDP 483 and is shown diagramatically in Figure 4. The construct was designated pZen 1677 (also known as pICI 1677; NCIMB 40773).

**1.3 Fermentation process for procathepsin L-6His**

*E.coli* strain MSD 213 was transformed with plasmid pZen 1677 and the resultant strain MSD 2148 (MSD 213 pZen 1677; NCIMB No 40773) stored as a glycerol stock at -80°C. An aliquot of MSD 213 pZen 1677 was streaked onto agar plates of L-tetracycline to separate single colonies after overnight growth at 37°C. A single colony of MSD 213 pZen 1677 was removed and resuspended in a 10ml L-tetracycline broth and 100µl immediately inoculated into each of seven 250ml Erlenmeyer flasks containing 75ml of L-tetracycline broth. After growth for 15h at 37°C on a reciprocating shaker the contents of the flasks were pooled and used to inoculate a single fermenter containing 15L of the growth medium described in the Table below.

**Table - Growth medium**

| Component | Concentration g/L deionized water |
|---|---|
| Potassium dihydrogen orthophosphate | 3.0 |
| di-Sodium hydrogen orthophosphate | 6.0 |
| Sodium chloride | 0.5 |
| Casein hydrolysate (Oxoid L.41) | 2.0 |
| Ammonium sulphate | 10.0 |
| Glycerol | 35.0 |
| Yeast Extract (Difco) | 20.0 |
| Magnesium sulphate 7-hydrate | 0.5 |
| Calcium chloride 2-hydrate | 0.03 |
| Thiamine | 0.008 |
| Iron sulphate 7-hydrate/Citric acid | 0.04/0.02 |
| Trace element solution (TES)* | 0.5ml/L |
| Tetracycline | (10mg/L) |

*Trace metal solution (TES)

| Component | mg/10ml deionized water |
|---|---|
| $AlCl_3.6H_2O$ | 2.0 |
| $CoCl_2.6H_2O$ | 0.8 |
| $KCr(SO_4)_2.12H_2O$ | 0.2 |
| $CuCl_2.2H_2O$ | 0.2 |
| $H_3BO_3$ | 0.1 |
| KI | 2.0 |
| $MnSO_4.H_2O$ | 2.0 |
| $NiSO_4.6H_2O$ | 0.09 |
| $Na_2MoO_4.2H_2O$ | 0.4 |
| $ZnSO_4.7H_2O$ | 0.4 |

The fermentation was carried out at a temperature of 37°C and pH, controlled by automatic addition of 6M sodium hydroxide and 2M sulphuric acid solutions, of pH 6.7. The dissolved oxygen tension (dOT) set-point was 50% air saturation and was controlled by automatic adjustment of the fermenter stirrer speed. Air flow to the fermenter was 20L/min corresponding to 1.33 volume volume per minute (VVM). A solution of yeast extract (stock 900g/4L) was fed into the fermenter at a rate of 190ml/h from 4,5h post inoculation. When the culture $OD_{550}$ reached ca. 40-45 (6h post inoculation), the fermentation temperature was decreased to 25°C and the fermentation continued at this temperature under the conditions described above for a further 1h.

When the culture $OD_{550}$ reached ca. 50-55 (7h post inoculation) procathepsin L-6His expression/secretion was induced by adding 75g L-arabinose to the fermenter (150ml of 50% stock). The fermentation was continued under these conditions until the supply of carbon source (glycerol) in the fermentation became exhausted (9h post inoculation) leading to a rapid rise in the dOT from 50% air saturation. At this point, a feed containing glycerol (714 g/L) and ammonium sulphate (143 g/L) was fed pumped into the fermenter. The rate at which this feed was supplied was adjusted to restrict the bacterial oxygen uptake rate (OUR) to approximately 80% of the fermenters maximum oxygen transfer rate (OTR), under the conditions described, whilst first returning and then maintaining the dOT at 50% air saturation. The fermentation was continued under these conditions until about

56h post fermenter inoculation when the culture was harvested by transferring aliquots of the fermenter contents into 1L centrifuge bottles.

The spent medium was separated from the bacterial cells by centrifugation in a Sorvall™ RC-3B centrifuge (7000x g, 4°C, 30min). Accumulation of procathepsin L-6His in the spent growth medium, and periplasm (extracts prepared using osmotic shock) was determined using SDS-PAGE followed by western blotting using an anti-Cathepsin L antibody as the primary antibody.

**1.4 Purification of cathepsin L-6His**

*E. coli* broth ( MSD 2148; NCIMB no 40773) was harvested by centrifugation at 5000 rpm for 30 min in a H 6000A rotor (Sorvall Instruments). All procedures were carried out at 4°C except where stated. The pellet was discarded while the supernatant (10 litres) was concentrated to 1 litre and dialysed with 15 litres of 20 mM Tris.HCl pH 7.0 in a spiral cartridge (Amicon™). The retentate was centrifuged at 12,000 rpm for 30 min in a GSA™ rotor (Sorvall Instruments). The pellet was discarded and the supernatant was further centrifuged for 35,000 rpm for 30 min in a 45 Ti rotor (Beckman Instruments).

The pellet was discarded and the supernatant was applied to a 1.5 cm x 3 cm $Ni^{2+}$ Nitrilo-tri-acetic acid-agarose column (QiaGen™) (flow rate 1 ml/min) equilibrated with 20 mM Tris.HCl pH 7.0. The unbound protein was collected and applied to a second 1.5 cm x 11 cm NTA column equilibrated with the the above buffer. Both columns were washed with 20 mM Tris.HCl pH 7.0, followed by 300 mM NaCl, 20 mM Tris.HCl pH 7.0, then 300 mM NaCl, sodium acetate pH 6.0 and finally eluted with 500 mM imidazole, sodium acetate pH 6.0. The two eluates (final pH 6.3) were pooled (protein concentration 1.3 mg/ml) and dialysed against 3 x 5 litres 20 mM sodium acetate pH 5.8 over 72 h. As a precipitate formed on dialysis, the combined eluates were centrifuged at 35,000 rpm for 30 min in a 45 Ti rotor™ (Beckman). The pellet (P) fraction was collected (note this material resulted in the isolation of cathepsin L-6His which surprisingly *could* be crystallised whilst cathepsin from the soluble fraction could not).

The P fraction was resuspended in 20 mM Tris.HCl pH 7.0, incubated for 48 h, spun at 35,000 rpm for 30 min in a 45 Ti rotor™ and then treated at pH 4 for 60 min at 22°C. The solution was subsequently dialysed against 20 mM sodium acetate pH 5.5 . The dialysate was applied to an ion exchange column (CM Fractogel™ (E. Merck/BDH),

1.5 cm x 11 cm, flow rate 1.0 ml/min) equilibrated with 20 mM sodium acetate pH 5.5, washed with 20 mM sodium acetate pH 5.5 and eluted with a gradient of 0-500 mM sodium chloride in 20 mM sodium acetate pH 5.5. The fractions were assayed using a Z-Phe-Arg-NHMec assay and the active fractions were pooled and subsequently treated at pH 4 for 60 min at 22°C. The pool was frozen at - 20°C.

Samples were thawed to 4°C and dialysed against sodium acetate pH 4.4 (3 x 5 litres) overnight and finally stored at - 20°C.

**1.5 Z-Phe-Arg-NHMec assay for cathepsin L-6His**

Cathepsin L-6His protein was incubated at 37°C for 30 min with the substrate 20µM Z-Phe-Arg-NHMec in an incubation buffer (total incubation volume = 175µl). The reaction was stopped with 175µl stop buffer. The sample was excited at 370 nm, and the emitted fluorescence was measured at 460 nm. Incubation buffer comprises: 88 mM $KH_2PO_4$, 12 mM $Na_2HPO_4$, 1 mM EDTA (disodium salt), 0.1% Brij 35 and 1 mM cysteine. Stop buffer comprises: 5.75 ml glacial acetic acid and, 11.6 g sodium chloracetate per litre water adjusted pH to 4.3 with NaOH. Results are expressed as nmoles of product formed per min normalised per mg of protein present (as measured by the Bradford method).

**Example 2 - Crystallisation and Structure Determination**

This work was performed on mature "clipped" cathepsin L i.e. in two-chain form, 175 amino acids and 42 amino acids, linked by a disulfide bridge with 3 residues being chopped off when the mature form was clipped.

Samples of purified cathepsin L (from Example 1.4) were thawed and concentrated on a Centricon C-10™ centrifuge filtration device (Amicon) using a GA-10 rotor™ operating at 5000 rpm at 10°C until final protein concentration as determined by Bradford method was 10 mg/ml. No crystals resulted, but initial indications for probable crystallisation conditions were found using the commercially available Hampton™ screening conditions (Jancaric, J & Kim, S.H. J. Appl. Cryst. 1991, 24, 409-411) on a Douglas Instruments Impax V ™ crystallisation robot, which prepares small drops under oil using the batch crystallisation method (McPherson, A. 1982. *Preparation and analysis of protein crystals*. John Wiley & Sons, New York). Crystallisation conditions were then found and optimised manually using trays of hanging drop vapour diffusion experiments

(McPherson, A. 1982. *Preparation and analysis of protein crystals*. John Wiley & Sons, New York). Best results were obtained when 4 µL of protein solution were dispensed onto siliclad coverslips and carefuly mixed with an equal volume of reservoir solution (100mM cacodylate buffer at pH6.2 containing 30% 2-methylpentan-2,4-diol). The coverslips were inverted and the drop were suspended over wells containing 950 µL of reservoir solution. The hanging drop experiments were equilibrated at 4°C. Wedge-shaped crystals appeared after 2-4 days and grew to their full size, typically 0.1 $mm^3$, within 7 days.

**2.1 Data collection and processing**

The crystallisation conditions fortuitously also functioned as cryoprotectant since they contained 30% methylpentandiol (MPD). This means the crystals could be flash frozen in a cold nitrogen stream at 100°K using the a cryostream cooler (Oxford Cryosystems™), thereby protecting the crystal against radiation damage, which was considered important given the small size of the crystals. A frozen crystal diffracted X-rays to 2Å resolution. Intensity data were recorded on a 30cm Imaging Plate (MarResearch) positioned 150mm away from the crystal. X-rays were generated by a rotating anode generator (Enraf-Nonius FR571™) operating at 40 kV and 90 mA, producing graphite monochromatised CuKα X-radiation. Images of 1° of crystal rotation were recorded with 30 minutes exposure. After a number of images were collected, the autoindexing routines in XDS software™ (Kabsch, W. 1988. Acta Cryst A21, 916-924) adapted for use with the MAR image plate were used to determine the symmetry and unit cell dimensions of the crystal. These were consistent with the monoclinic space group $P2_1$, with $a$ = 46.23, $b$ = 49.38, $c$ = 49.25 Å and β = 113.45°. The presence of a single molecule of cathepsin L in the asymmetric unit corresponds to a volume to mass ratio of $V_M$=2.1 $Å^3$/Da, or a solvent content of about 40% in the crystal. The data collection was continued for 5 days on a single crystal, which would probably not have been possible without freezing the crystal. The 27496 intensity data were merged across equivalent reflections to give 12421 unique reflection intensities using the program MARSCALE. The overall $R_{merge}$ was 6.0% for all data between 15 and 2Å, while in the highest resolution shell (2.4-2.0Å) $R_{merge}$ was 11.9%. The intensity data were reduced to structure amplitudes using the program TRUNCATE in the CCP4 suite (CCP4, 1994, Acta Cryst D50, 760-763).

## 2.2 Structure s lution and refinement

Since there is 40% amino acid identity with papain, a well-refined papain model was thought to be a suitable trial model for molecular replacement. Three variations of the trial model were created: firstly a full papain model (Brookhaven Data Bank entry 9PAP), secondly the papain model with side chains truncated to the least common demoninator and insertions with respect to cathepsin L deleted, and thirdly a homology model of cathepsin L built from the papain structure and energy minimised.

The program AMORE as available from the CCP4 suite of protein crystallography programs (CCP4, 1994, Acta Cryst D51, 760-763) was used for the molecular replacement. Structure factors for the trial models were calculated in a cubic cell of 80 Å. The molecular replacement was carried out using all data between the resolution limits 10 and 4Å within a Patterson integration radius of 25Å. The three trial models gave Rotation function values of 24, 23 and 21, respectively, which were over twice the value of the next highest peak in the rotation function maps. Following the translation function, the correlation between observed and calculated data were, for the three trial models, 0.395, 0.440 and 0.355 respectively, while the crystallographic R-values were 46.6, 46.0 and 48.8%, for the full papain, trimmed papain, and homology model respectively.

Inspection with computer graphics showed that papain molecules rotated and translated to these molecular replacement solutions packed well into the unit cell without any interpenetration of neighbouring molecules. The full papain and trimmed papain models gave equivalent solutions, while the homology model had positioned the molecule correctly but upside down relative to the papain models. Attempts to refine the homology model solution were not succesful. The trimmed papain molecule, rotated and translated from the Brookhaven data bank coordinates (entry 9PAP) by the eulerian angles $\alpha$ = 235.63, $\beta$ = 168.58, and $\gamma$ = 95.75° and by the fractional coordinates 0.160166, 0.0, -0.27854, was taken for further work.

This model was refined using the program XPLOR™ and the standard simulated annealing protocol suggested by Bruenger (Bruenger, 1988, J.Mol. Biol. 203, 803-816). The refinement used all data between 10 and 2Å. After the first round of refinement, R was 35%, but the $R_{free}$ still around 43%, suggesting considerable model bias. Inspection of a 2Fo-Fc electron density map showed that while part of the model fit the density well there

were also large portions of the molecule where the agrement with the density was poor. However, the solution was und ubtedly correct since exceptionally clear sidechain density for several aromatic amino acid residues was visible where as the model had been truncated to Cβ in these cases.

As much of the electron density was interpreted as possible and those portions where the interpretation was not clear were omitted from the model altogether before refinement continued. The model consisted of 6 segments at the next round of refinement. A second round of simulated annealing refinement using XPLOR™ resulted in R = 37% and $R_{free}$ = 44%, however the electron density map now shows clearly the positions of many side chains and of some of the loops that were previously omitted, although there still remained some 30 residues which have not been built correctly yet. The model was again subjected to simulated annealing resulting in R=34% to 2Å. The resultant electron density map now shows all missing loops. Individual isotropic atomic temperature factors have been applied and solvent water molecules have been added to the model. This results in an accurate structure (2Å) of cathepsin-L. The coordinates of the model are set out in Example 4. This model has R=21% with 157 solvent water molecules included.

**Example 3: Use of the cathepsin L structure in structure-based drug design**

Having determined the coordinates for the atomic structure of cathepsin L, as well as having devised the crystallisation protocol for cathepsin L, we are now in a strong position to design drugs against the disease targets that involve cathepsin L, such as bone resorption and osteoporosis. The approaches used for this include the following.

(1) We superpose our cathepsin L coordinates onto other available coordinates of thiol proteases which have inhibitors bound to give us a first approximation of the way these and related inhibitors might bind cathepsin. The active site of cathepsin is very similar to that of papain for example, as might be expected from sequence homology. However, inhibitors of papain such as leupeptin extend to a region of the protease where the homology begins to break down, and these different areas in the protein confer different binding modes for the inhibitors which can be modelled. We can see which parts of the inhibitors can be modified without affecting the interactions the inhibitor makes with the protein; it is these modifications that can be used to adjust the physical properties of the

inhibitor without affecting the binding. We can also predict modifications of the inhibitor which lead to stronger interactions with the protein; this is rational optimisation of a lead compound. Such predictions are made in conference with medicinal chemists who assess the feasibility of synthesis - this allows us to generate compounds that can be tested in activity assays and which may be complexed with the cathepsin crystals allowing rapid X-ray determination of the complex structure.

(2) Using our coordinates for the cathepsin L molecule, we use a variety of available ligand design software to generate pharmacophore models that are specific for binding at the cathepsin L active site. These in turn can be used to search real and virtual compound data bases to provide a list of possible candidate inhibitors that match the pharmacophore. Another way to generate models of ligands is to "grow" them in the active site. The software used includes commercially available programs such as LUDI™ and LEAPFROG™.

LUDI™ examines interactions of molecular fragments from a data base with the protein active site, and allows the user to build up a chemically realistic molecule from suitable fragments.

LEAPFROG™ "grows" new ligands using a genetic algorithm, the parameters that direct the growth of the ligand being under the control of the user.

Compounds proposed by the ligand design software are synthesised and tested for activity. If active, they can be complexed with crystals of cathepsin L for structural analysis.

(3) An important step in the drug design cycle is the feedback of how a designed compound truly interacts with the protein, which can be done if a crystallisation protocol is in place. The crystals can be soaked in a solution of the inhibitor for 24 hours before collecting the X-ray diffraction patterns. A (complex-native) difference Fourier synthesis using the phases derived from the native protein crystal structure is a straight forward calculation which rapidly gives the electron density at atomic resolution for the inhibitor, showing exactly where and how it binds. Alternatively, the crystals can be grown in the presence of the inhibitor. The crystal structure of the inhibitor complex is useful in many ways, for example, it allows us to examine unambiguously the interactions that the inhibitor makes with the protein so that we can enter a new cycle of rational improvement,

and it also enables us to identify parts of the molecule which may be modified in order to alter physical proerties without compromising binding in order to improve *in vivo* activity. Importantly, it allows us to learn how well our intended optimisations resemble what actually occurs in the crystal, so that we may refine further our own ability to design optimised inhibitor-protein interactions.

(4) Inhibitors found by random screening can be optimised rationally as in (3).

(5) The inhibitors found from two different chemical series by any of the above methods can be combined rationally to produce hybrid compounds that incorporate the protein interactions seen in both series of inhibitors to maximum effect.

(6) Inhibitors found using the above methods are analysed structurally to arrive at ways of generating diversity through the use of carefully designed chemical libraries. In this way, larger numbers of substituents can be tested for activity and additional compounds of interest can be optimised further by re-entering them in the rational design cycle.

Inhibitors identified using the above methods are analysed further in assays including *in vivo* assays.

Example 4

**Coordinates for Cathepsin L**

```
CRYSTL   46.430   49.380   49.250  90.00 113.45  90.00     1
SCALE1      0.021538  0.000000  0.009343        0.000000
SCALE2      0.000000  0.020251  0.000000        0.000000
SCALE3      0.000000  0.000000  0.022133        0.000000
ATOM      1  CB  ALA A   1      -0.877  21.216  12.640  1.00 27.20
ATOM      2  C   ALA A   1      -1.316  22.399  10.477  1.00 26.12
ATOM      3  O   ALA A   1      -2.175  23.276  10.518  1.00 27.83
ATOM      4  N   ALA A   1      -0.251  23.588  12.251  1.00 28.44
ATOM      5  CA  ALA A   1      -0.342  22.242  11.626  1.00 26.83
ATOM      6  N   PRO A   2      -1.145  21.617   9.400  1.00 23.75
ATOM      7  CD  PRO A   2      -0.077  20.646   9.107  1.00 22.84
ATOM      8  CA  PRO A   2      -2.071  21.736   8.271  1.00 21.66
ATOM      9  CB  PRO A   2      -1.442  20.821   7.220  1.00 21.82
ATOM     10  CG  PRO A   2       0.014  20.739   7.623  1.00 22.38
ATOM     11  C   PRO A   2      -3.447  21.218   8.691  1.00 20.10
ATOM     12  O   PRO A   2      -3.625  20.729   9.802  1.00 18.59
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ATOM     13  N   ARG A   3      -4.436  21.357   7.821  1.00 19.96
ATOM     14  CA  ARG A   3      -5.766  20.857   8.152  1.00 21.14
ATOM     15  CB  ARG A   3      -6.874  21.772   7.577  1.00 24.00
ATOM     16  CG  ARG A   3      -6.892  23.174   8.259  1.00 28.09
ATOM     17  CD  ARG A   3      -8.252  23.863   8.215  1.00 30.40
ATOM     18  NE  ARG A   3      -8.696  24.080   6.840  1.00 32.98
ATOM     19  CZ  ARG A   3      -9.915  23.796   6.388  1.00 33.51
ATOM     20  NH1 ARG A   3     -10.831  23.280   7.208  1.00 33.09
ATOM     21  NH2 ARG A   3     -10.211  24.009   5.105  1.00 33.81
ATOM     22  C   ARG A   3      -5.913  19.387   7.718  1.00 17.20
ATOM     23  O   ARG A   3      -6.685  18.629   8.302  1.00 16.72
ATOM     24  N   SER A   4      -5.125  18.999   6.723  1.00 14.03
ATOM     25  CA  SER A   4      -5.107  17.646   6.197  1.00 11.83
ATOM     26  CB  SER A   4      -5.728  17.601   4.802  1.00 11.68
ATOM     27  OG  SER A   4      -7.126  17.827   4.870  1.00 15.44
ATOM     28  C   SER A   4      -3.656  17.219   6.087  1.00  9.98
ATOM     29  O   SER A   4      -2.792  18.029   5.745  1.00  8.83
ATOM     30  N   VAL A   5      -3.387  15.960   6.407  1.00  8.94
ATOM     31  CA  VAL A   5      -2.044  15.402   6.312  1.00  9.62
ATOM     32  CB  VAL A   5      -1.311  15.383   7.684  1.00  8.56
ATOM     33  CG1 VAL A   5      -0.101  14.476   7.597  1.00  9.25
ATOM     34  CG2 VAL A   5      -0.860  16.787   8.085  1.00  8.49
ATOM     35  C   VAL A   5      -2.177  13.970   5.823  1.00  9.02
ATOM     36  O   VAL A   5      -3.069  13.257   6.284  1.00 10.58
ATOM     37  N   ASP A   6      -1.315  13.573   4.888  1.00  7.29
ATOM     38  CA  ASP A   6      -1.292  12.212   4.348  1.00  7.93
ATOM     39  CB  ASP A   6      -2.235  12.040   3.145  1.00  7.36
ATOM     40  CG  ASP A   6      -2.443  10.571   2.760  1.00  8.26
ATOM     41  OD1 ASP A   6      -1.756   9.679   3.294  1.00  8.11
ATOM     42  OD2 ASP A   6      -3.298  10.302   1.913  1.00  9.91
ATOM     43  C   ASP A   6       0.128  11.869   3.929  1.00  7.11
ATOM     44  O   ASP A   6       0.528  12.109   2.787  1.00  5.38
ATOM     45  N   TRP A   7       0.830  11.174   4.817  1.00  6.66
ATOM     46  CA  TRP A   7       2.207  10.800   4.561  1.00  5.18
ATOM     47  CB  TRP A   7       2.871  10.293   5.844  1.00  5.63
ATOM     48  CG  TRP A   7       3.106  11.375   6.857  1.00  3.75
ATOM     49  CD2 TRP A   7       4.099  12.415   6.796  1.00  5.24
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ATOM     50  CE2 TRP A   7       3.992  13.165   7.984  1.00  2.70
ATOM     51  CE3 TRP A   7       5.075  12.776   5.852  1.00  4.91
ATOM     52  CD1 TRP A   7       2.449  11.548   8.047  1.00  3.93
ATOM     53  NE1 TRP A   7       2.978  12.618   8.725  1.00  2.42
ATOM     54  CZ2 TRP A   7       4.823  14.250   8.260  1.00  3.41
ATOM     55  CZ3 TRP A   7       5.899  13.855   6.131  1.00  3.27
ATOM     56  CH2 TRP A   7       5.765  14.577   7.324  1.00  3.02
ATOM     57  C   TRP A   7       2.384   9.826   3.415  1.00  6.34
ATOM     58  O   TRP A   7       3.511   9.628   2.961  1.00  6.00
ATOM     59  N   ARG A   8       1.288   9.221   2.939  1.00  7.07
ATOM     60  CA  ARG A   8       1.360   8.301   1.801  1.00  7.88
ATOM     61  CB  ARG A   8       0.018   7.613   1.510  1.00  6.47
ATOM     62  CG  ARG A   8      -0.364   6.530   2.495  1.00  9.08
ATOM     63  CD  ARG A   8      -1.711   5.920   2.164  1.00  9.74
ATOM     64  NE  ARG A   8      -2.776   6.919   2.212  1.00 12.63
ATOM     65  CZ  ARG A   8      -4.024   6.724   1.787  1.00 13.43
ATOM     66  NH1 ARG A   8      -4.395   5.555   1.286  1.00 14.70
ATOM     67  NH2 ARG A   8      -4.889   7.730   1.797  1.00 15.31
ATOM     68  C   ARG A   8       1.767   9.093   0.577  1.00  9.94
ATOM     69  O   ARG A   8       2.504   8.607  -0.276  1.00 10.87
ATOM     70  N   GLU A   9       1.318  10.337   0.505  1.00 11.77
ATOM     71  CA  GLU A   9       1.640  11.189  -0.637  1.00 14.34
ATOM     72  CB  GLU A   9       0.759  12.442  -0.616  1.00 16.42
ATOM     73  CG  GLU A   9      -0.728  12.126  -0.802  1.00 19.57
ATOM     74  CD  GLU A   9      -1.647  13.323  -0.558  1.00 21.78
ATOM     75  OE1 GLU A   9      -1.218  14.309   0.096  1.00 22.24
ATOM     76  OE2 GLU A   9      -2.817  13.266  -1.008  1.00 23.66
ATOM     77  C   GLU A   9       3.116  11.576  -0.706  1.00 13.25
ATOM     78  O   GLU A   9       3.571  12.112  -1.719  1.00 15.61
ATOM     79  N   LYS A  10       3.867  11.282   0.351  1.00 11.63
ATOM     80  CA  LYS A  10       5.284  11.613   0.393  1.00 11.92
ATOM     81  CB  LYS A  10       5.572  12.522   1.592  1.00 10.96
ATOM     82  CG  LYS A  10       4.880  13.872   1.461  1.00 11.07
ATOM     83  CD  LYS A  10       5.408  14.884   2.421  1.00  9.57
ATOM     84  CE  LYS A  10       4.714  16.219   2.224  1.00 10.48
ATOM     85  NZ  LYS A  10       5.081  17.093   3.357  1.00 12.29
ATOM     86  C   LYS A  10       6.274  10.450   0.334  1.00 11.29
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ATOM     87  O   LYS A  10       7.466  10.662   0.499  1.00 13.17
ATOM     88  N   GLY A  11       5.787   9.231   0.098  1.00 12.10
ATOM     89  CA  GLY A  11       6.663   8.062   0.011  1.00  8.89
ATOM     90  C   GLY A  11       7.111   7.421   1.321  1.00  8.67
ATOM     91  O   GLY A  11       8.036   6.614   1.319  1.00  8.22
ATOM     92  N   TYR A  12       6.425   7.753   2.417  1.00  5.70
ATOM     93  CA  TYR A  12       6.714   7.270   3.772  1.00  4.43
ATOM     94  CB  TYR A  12       6.166   8.304   4.755  1.00  5.23
ATOM     95  CG  TYR A  12       7.068   9.466   5.081  1.00  4.74
ATOM     96  CD1 TYR A  12       7.405  10.416   4.120  1.00  5.67
ATOM     97  CE1 TYR A  12       8.183  11.526   4.449  1.00  6.04
ATOM     98  CD2 TYR A  12       7.528   9.645   6.375  1.00  6.11
ATOM     99  CE2 TYR A  12       8.300  10.740   6.720  1.00  8.08
ATOM    100  CZ  TYR A  12       8.621  11.680   5.752  1.00  8.16
ATOM    101  OH  TYR A  12       9.355  12.783   6.123  1.00 11.13
ATOM    102  C   TYR A  12       6.099   5.913   4.209  1.00  4.43
ATOM    103  O   TYR A  12       6.466   5.367   5.271  1.00  2.69
ATOM    104  N   VAL A  13       5.144   5.407   3.426  1.00  2.65
ATOM    105  CA  VAL A  13       4.400   4.194   3.783  1.00  3.43
ATOM    106  CB  VAL A  13       2.902   4.563   4.072  1.00  3.74
ATOM    107  CG1 VAL A  13       2.185   3.449   4.832  1.00  5.21
ATOM    108  CG2 VAL A  13       2.806   5.871   4.843  1.00  2.23
ATOM    109  C   VAL A  13       4.422   3.037   2.785  1.00  2.70
ATOM    110  O   VAL A  13       4.258   3.216   1.568  1.00  2.00
ATOM    111  N   THR A  14       4.611   1.834   3.309  1.00  3.78
ATOM    112  CA  THR A  14       4.607   0.648   2.471  1.00  2.88
ATOM    113  CB  THR A  14       5.360  -0.520   3.119  1.00  2.00
ATOM    114  OG1 THR A  14       4.865  -0.733   4.443  1.00  2.99
ATOM    115  CG2 THR A  14       6.855  -0.273   3.110  1.00  2.00
ATOM    116  C   THR A  14       3.164   0.203   2.284  1.00  2.85
ATOM    117  O   THR A  14       2.263   0.623   3.016  1.00  4.31
ATOM    118  N   PRO A  15       2.926  -0.647   1.287  1.00  3.14
ATOM    119  CD  PRO A  15       3.863  -1.097   0.237  1.00  3.37
ATOM    120  CA  PRO A  15       1.572  -1.141   1.035  1.00  3.31
ATOM    121  CB  PRO A  15       1.796  -2.151  -0.082  1.00  3.57
ATOM    122  CG  PRO A  15       2.930  -1.516  -0.862  1.00  2.31
ATOM    123  C   PRO A  15       1.001  -1.804   2.278  1.00  4.50
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ATOM    124  O   PRO A  15       1.730  -2.147   3.225  1.00  7.69
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ATOM    126  CA  VAL A  16      -0.951  -2.561   3.439  1.00  4.19
ATOM    127  CB  VAL A  16      -2.460  -2.467   3.285  1.00  4.60
ATOM    128  CG1 VAL A  16      -3.181  -3.317   4.329  1.00  5.37
ATOM    129  CG2 VAL A  16      -2.865  -1.019   3.440  1.00  5.35
ATOM    130  C   VAL A  16      -0.476  -4.018   3.538  1.00  4.85
ATOM    131  O   VAL A  16      -0.230  -4.661   2.521  1.00  2.91
ATOM    132  N   LYS A  17      -0.246  -4.480   4.768  1.00  5.25
ATOM    133  CA  LYS A  17       0.186  -5.859   5.035  1.00  5.74
ATOM    134  CB  LYS A  17       1.448  -5.867   5.891  1.00  6.60
ATOM    135  CG  LYS A  17       2.670  -5.316   5.171  1.00  5.83
ATOM    136  CD  LYS A  17       3.769  -5.064   6.139  1.00  5.40
ATOM    137  CE  LYS A  17       4.928  -4.378   5.459  1.00  7.08
ATOM    138  NZ  LYS A  17       5.991  -4.112   6.466  1.00  4.70
ATOM    139  C   LYS A  17      -0.932  -6.634   5.742  1.00  6.36
ATOM    140  O   LYS A  17      -2.000  -6.090   5.995  1.00  6.25
ATOM    141  N   ASN A  18      -0.699  -7.904   6.053  1.00  7.06
ATOM    142  CA  ASN A  18      -1.724  -8.717   6.715  1.00  8.00
ATOM    143  CB  ASN A  18      -2.471  -9.555   5.675  1.00  9.18
ATOM    144  CG  ASN A  18      -3.767 -10.120   6.210  1.00  9.76
ATOM    145  OD1 ASN A  18      -3.947 -10.239   7.430  1.00 11.21
ATOM    146  ND2 ASN A  18      -4.701 -10.440   5.303  1.00 10.47
ATOM    147  C   ASN A  18      -1.095  -9.612   7.792  1.00  7.45
ATOM    148  O   ASN A  18      -0.224 -10.433   7.515  1.00  9.35
ATOM    149  N   GLN A  19      -1.530  -9.436   9.024  1.00  7.64
ATOM    150  CA  GLN A  19      -0.975 -10.187  10.143  1.00  8.88
ATOM    151  CB  GLN A  19      -1.239  -9.438  11.458  1.00  6.97
ATOM    152  CG  GLN A  19      -2.703  -9.348  11.796  1.00  8.46
ATOM    153  CD  GLN A  19      -2.995  -8.525  13.021  1.00  8.38
ATOM    154  OE1 GLN A  19      -3.096  -7.307  12.951  1.00 11.05
ATOM    155  NE2 GLN A  19      -3.197  -9.190  14.147  1.00  9.98
ATOM    156  C   GLN A  19      -1.501 -11.629  10.243  1.00 10.55
ATOM    157  O   GLN A  19      -0.978 -12.426  11.023  1.00 10.56
ATOM    158  N   GLY A  20      -2.528 -11.951   9.461  1.00 11.52
ATOM    159  CA  GLY A  20      -3.120 -13.282   9.505  1.00 14.78
ATOM    160  C   GLY A  20      -3.689 -13.642  10.876  1.00 16.31
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ATOM    162  N   GLN A  21      -3.663 -14.933  11.191  1.00 18.50
ATOM    163  CA  GLN A  21      -4.146 -15.474  12.463  1.00 21.24
ATOM    164  CB  GLN A  21      -4.640 -16.915  12.248  1.00 24.70
ATOM    165  CG  GLN A  21      -6.094 -17.040  11.789  1.00 28.58
ATOM    166  CD  GLN A  21      -7.086 -16.847  12.936  1.00 31.08
ATOM    167  OE1 GLN A  21      -6.907 -17.390  14.034  1.00 32.46
ATOM    168  NE2 GLN A  21      -8.141 -16.070  12.683  1.00 31.53
ATOM    169  C   GLN A  21      -3.033 -15.448  13.519  1.00 19.56
ATOM    170  O   GLN A  21      -2.633 -16.485  14.067  1.00 21.26
ATOM    171  N   CYS A  22      -2.503 -14.259  13.764  1.00 15.59
ATOM    172  CA  CYS A  22      -1.433 -14.074  14.730  1.00 11.69
ATOM    173  C   CYS A  22      -1.636 -12.682  15.350  1.00 11.27
ATOM    174  O   CYS A  22      -1.967 -11.724  14.643  1.00 10.21
ATOM    175  CB  CYS A  22      -0.082 -14.196  14.011  1.00 10.01
ATOM    176  SG  CYS A  22       1.384 -13.661  14.947  1.00  9.82
ATOM    177  N   GLY A  23      -1.569 -12.599  16.675  1.00 10.96
ATOM    178  CA  GLY A  23      -1.750 -11.327  17.359  1.00  9.90
ATOM    179  C   GLY A  23      -0.460 -10.528  17.340  1.00  7.69
ATOM    180  O   GLY A  23       0.146 -10.290  18.382  1.00  5.44
ATOM    181  N   SER A  24      -0.066 -10.111  16.139  1.00  6.31
ATOM    182  CA  SER A  24       1.172  -9.369  15.916  1.00  6.11
ATOM    183  CB  SER A  24       2.017 -10.147  14.919  1.00  3.13
ATOM    184  OG  SER A  24       1.220 -10.487  13.804  1.00  2.22
ATOM    185  C   SER A  24       0.952  -7.939  15.390  1.00  5.17
ATOM    186  O   SER A  24       1.857  -7.348  14.817  1.00  4.46
ATOM    187  N   CYS A  25      -0.244  -7.395  15.602  1.00  6.02
ATOM    188  CA  CYS A  25      -0.576  -6.041  15.148  1.00  8.54
ATOM    189  CB  CYS A  25      -1.987  -5.644  15.612  1.00 10.76
ATOM    190  SG  CYS A  25      -2.253  -5.670  17.388  1.00 16.00
ATOM    191  C   CYS A  25       0.451  -5.046  15.678  1.00  7.98
ATOM    192  O   CYS A  25       0.840  -4.093  14.995  1.00  6.80
ATOM    193  N   TRP A  26       0.912  -5.306  16.900  1.00  6.81
ATOM    194  CA  TRP A  26       1.910  -4.475  17.542  1.00  5.51
ATOM    195  CB  TRP A  26       2.227  -5.017  18.942  1.00  5.06
ATOM    196  CG  TRP A  26       2.707  -6.451  18.963  1.00  5.62
ATOM    197  CD2 TRP A  26       4.071  -6.907  18.857  1.00  4.05
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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 198 | CE2 | TRP | A | 26 | 4.044 | -8.320 | 18.906 | 1.00 | 3.12 |
| ATOM | 199 | CE3 | TRP | A | 26 | 5.308 | -6.256 | 18.721 | 1.00 | 2.00 |
| ATOM | 200 | CD1 | TRP | A | 26 | 1.933 | -7.579 | 19.068 | 1.00 | 4.02 |
| ATOM | 201 | NE1 | TRP | A | 26 | 2.732 | -8.697 | 19.031 | 1.00 | 5.11 |
| ATOM | 202 | CZ2 | TRP | A | 26 | 5.210 | -9.102 | 18.829 | 1.00 | 3.13 |
| ATOM | 203 | CZ3 | TRP | A | 26 | 6.474 | -7.044 | 18.639 | 1.00 | 2.32 |
| ATOM | 204 | CH2 | TRP | A | 26 | 6.408 | -8.449 | 18.696 | 1.00 | 2.00 |
| ATOM | 205 | C | TRP | A | 26 | 3.177 | -4.415 | 16.679 | 1.00 | 5.29 |
| ATOM | 206 | O | TRP | A | 26 | 3.841 | -3.384 | 16.625 | 1.00 | 3.85 |
| ATOM | 207 | N | ALA | A | 27 | 3.483 | -5.514 | 15.990 | 1.00 | 3.57 |
| ATOM | 208 | CA | ALA | A | 27 | 4.661 | -5.594 | 15.130 | 1.00 | 3.43 |
| ATOM | 209 | CB | ALA | A | 27 | 5.094 | -7.082 | 14.916 | 1.00 | 2.00 |
| ATOM | 210 | C | ALA | A | 27 | 4.469 | -4.865 | 13.802 | 1.00 | 2.20 |
| ATOM | 211 | O | ALA | A | 27 | 5.410 | -4.267 | 13.305 | 1.00 | 3.00 |
| ATOM | 212 | N | PHE | A | 28 | 3.262 | -4.908 | 13.229 | 1.00 | 2.67 |
| ATOM | 213 | CA | PHE | A | 28 | 2.983 | -4.215 | 11.968 | 1.00 | 3.09 |
| ATOM | 214 | CB | PHE | A | 28 | 1.677 | -4.714 | 11.320 | 1.00 | 2.99 |
| ATOM | 215 | CG | PHE | A | 28 | 1.801 | -6.090 | 10.688 | 1.00 | 2.39 |
| ATOM | 216 | CD1 | PHE | A | 28 | 1.810 | -7.236 | 11.483 | 1.00 | 2.92 |
| ATOM | 217 | CD2 | PHE | A | 28 | 2.011 | -6.227 | 9.318 | 1.00 | 2.00 |
| ATOM | 218 | CE1 | PHE | A | 28 | 2.036 | -8.494 | 10.919 | 1.00 | 2.00 |
| ATOM | 219 | CE2 | PHE | A | 28 | 2.240 | -7.473 | 8.753 | 1.00 | 2.00 |
| ATOM | 220 | CZ | PHE | A | 28 | 2.255 | -8.604 | 9.550 | 1.00 | 2.00 |
| ATOM | 221 | C | PHE | A | 28 | 2.914 | -2.705 | 12.217 | 1.00 | 3.35 |
| ATOM | 222 | O | PHE | A | 28 | 3.281 | -1.903 | 11.355 | 1.00 | 5.15 |
| ATOM | 223 | N | SER | A | 29 | 2.451 | -2.321 | 13.402 | 1.00 | 2.49 |
| ATOM | 224 | CA | SER | A | 29 | 2.366 | -0.909 | 13.760 | 1.00 | 2.00 |
| ATOM | 225 | CB | SER | A | 29 | 1.524 | -0.746 | 15.010 | 1.00 | 2.00 |
| ATOM | 226 | OG | SER | A | 29 | 1.394 | 0.609 | 15.394 | 1.00 | 2.70 |
| ATOM | 227 | C | SER | A | 29 | 3.779 | -0.368 | 13.980 | 1.00 | 2.00 |
| ATOM | 228 | O | SER | A | 29 | 4.114 | 0.720 | 13.505 | 1.00 | 4.83 |
| ATOM | 229 | N | ALA | A | 30 | 4.619 | -1.159 | 14.644 | 1.00 | 2.00 |
| ATOM | 230 | CA | ALA | A | 30 | 5.993 | -0.778 | 14.926 | 1.00 | 2.14 |
| ATOM | 231 | CB | ALA | A | 30 | 6.634 | -1.761 | 15.921 | 1.00 | 2.00 |
| ATOM | 232 | C | ALA | A | 30 | 6.838 | -0.650 | 13.664 | 1.00 | 2.00 |
| ATOM | 233 | O | ALA | A | 30 | 7.583 | 0.318 | 13.521 | 1.00 | 4.26 |
| ATOM | 234 | N | THR | A | 31 | 6.731 | -1.613 | 12.744 | 1.00 | 4.13 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 235 | CA | THR | A | 31 | 7.486 | -1.551 | 11.490 | 1.00 | 2.32 |
| ATOM | 236 | CB | THR | A | 31 | 7.417 | -2.870 | 10.668 | 1.00 | 2.61 |
| ATOM | 237 | OG1 | THR | A | 31 | 6.048 | -3.226 | 10.450 | 1.00 | 4.22 |
| ATOM | 238 | CG2 | THR | A | 31 | 8.186 | -4.038 | 11.357 | 1.00 | 2.00 |
| ATOM | 239 | C | THR | A | 31 | 6.923 | -0.398 | 10.632 | 1.00 | 2.96 |
| ATOM | 240 | O | THR | A | 31 | 7.660 | 0.233 | 9.869 | 1.00 | 2.64 |
| ATOM | 241 | N | GLY | A | 32 | 5.615 | -0.158 | 10.721 | 1.00 | 2.07 |
| ATOM | 242 | CA | GLY | A | 32 | 5.019 | 0.935 | 9.970 | 1.00 | 2.00 |
| ATOM | 243 | C | GLY | A | 32 | 5.638 | 2.259 | 10.379 | 1.00 | 2.00 |
| ATOM | 244 | O | GLY | A | 32 | 6.079 | 3.045 | 9.545 | 1.00 | 2.21 |
| ATOM | 245 | N | ALA | A | 33 | 5.686 | 2.493 | 11.683 | 1.00 | 2.47 |
| ATOM | 246 | CA | ALA | A | 33 | 6.286 | 3.694 | 12.260 | 1.00 | 2.46 |
| ATOM | 247 | CB | ALA | A | 33 | 6.055 | 3.706 | 13.762 | 1.00 | 2.00 |
| ATOM | 248 | C | ALA | A | 33 | 7.796 | 3.765 | 11.946 | 1.00 | 3.23 |
| ATOM | 249 | O | ALA | A | 33 | 8.282 | 4.826 | 11.585 | 1.00 | 2.50 |
| ATOM | 250 | N | LEU | A | 34 | 8.533 | 2.656 | 12.079 | 1.00 | 2.77 |
| ATOM | 251 | CA | LEU | A | 34 | 9.977 | 2.663 | 11.780 | 1.00 | 2.95 |
| ATOM | 252 | CB | LEU | A | 34 | 10.684 | 1.397 | 12.304 | 1.00 | 4.24 |
| ATOM | 253 | CG | LEU | A | 34 | 12.215 | 1.295 | 12.145 | 1.00 | 3.68 |
| ATOM | 254 | CD1 | LEU | A | 34 | 12.954 | 2.581 | 12.640 | 1.00 | 2.00 |
| ATOM | 255 | CD2 | LEU | A | 34 | 12.694 | 0.085 | 12.936 | 1.00 | 2.56 |
| ATOM | 256 | C | LEU | A | 34 | 10.263 | 2.861 | 10.296 | 1.00 | 2.58 |
| ATOM | 257 | O | LEU | A | 34 | 11.244 | 3.489 | 9.931 | 1.00 | 3.87 |
| ATOM | 258 | N | GLU | A | 35 | 9.392 | 2.340 | 9.442 | 1.00 | 2.37 |
| ATOM | 259 | CA | GLU | A | 35 | 9.549 | 2.496 | 8.001 | 1.00 | 3.81 |
| ATOM | 260 | CB | GLU | A | 35 | 8.467 | 1.700 | 7.251 | 1.00 | 4.26 |
| ATOM | 261 | CG | GLU | A | 35 | 8.723 | 0.181 | 7.159 | 1.00 | 4.41 |
| ATOM | 262 | CD | GLU | A | 35 | 7.475 | -0.626 | 6.916 | 1.00 | 6.77 |
| ATOM | 263 | OE1 | GLU | A | 35 | 6.373 | -0.047 | 6.741 | 1.00 | 6.95 |
| ATOM | 264 | OE2 | GLU | A | 35 | 7.587 | -1.865 | 6.896 | 1.00 | 7.64 |
| ATOM | 265 | C | GLU | A | 35 | 9.471 | 3.987 | 7.632 | 1.00 | 4.62 |
| ATOM | 266 | O | GLU | A | 35 | 10.244 | 4.462 | 6.788 | 1.00 | 4.48 |
| ATOM | 267 | N | GLY | A | 36 | 8.575 | 4.715 | 8.300 | 1.00 | 2.53 |
| ATOM | 268 | CA | GLY | A | 36 | 8.419 | 6.137 | 8.061 | 1.00 | 2.91 |
| ATOM | 269 | C | GLY | A | 36 | 9.614 | 6.927 | 8.559 | 1.00 | 4.17 |
| ATOM | 270 | O | GLY | A | 36 | 10.101 | 7.824 | 7.866 | 1.00 | 6.97 |
| ATOM | 271 | N | GLN | A | 37 | 10.107 | 6.594 | 9.748 | 1.00 | 3.54 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 272 | CA | GLN | A | 37 | 11.248 | 7.302 | 10.285 | 1.00 | 3.67 |
| ATOM | 273 | CB | GLN | A | 37 | 11.409 | 7.065 | 11.776 | 1.00 | 2.49 |
| ATOM | 274 | CG | GLN | A | 37 | 10.277 | 7.637 | 12.607 | 1.00 | 5.01 |
| ATOM | 275 | CD | GLN | A | 37 | 10.000 | 9.107 | 12.316 | 1.00 | 3.24 |
| ATOM | 276 | OE1 | GLN | A | 37 | 10.769 | 9.981 | 12.718 | 1.00 | 5.78 |
| ATOM | 277 | NE2 | GLN | A | 37 | 8.915 | 9.380 | 11.617 | 1.00 | 2.02 |
| ATOM | 278 | C | GLN | A | 37 | 12.537 | 7.016 | 9.537 | 1.00 | 6.45 |
| ATOM | 279 | O | GLN | A | 37 | 13.387 | 7.898 | 9.434 | 1.00 | 7.80 |
| ATOM | 280 | N | MET | A | 38 | 12.701 | 5.797 | 9.029 | 1.00 | 5.74 |
| ATOM | 281 | CA | MET | A | 38 | 13.896 | 5.460 | 8.257 | 1.00 | 7.86 |
| ATOM | 282 | CB | MET | A | 38 | 14.007 | 3.953 | 7.964 | 1.00 | 7.31 |
| ATOM | 283 | CG | MET | A | 38 | 14.406 | 3.093 | 9.147 | 1.00 | 6.19 |
| ATOM | 284 | SD | MET | A | 38 | 15.946 | 3.583 | 9.892 | 1.00 | 6.69 |
| ATOM | 285 | CE | MET | A | 38 | 16.960 | 3.664 | 8.429 | 1.00 | 2.57 |
| ATOM | 286 | C | MET | A | 38 | 13.837 | 6.233 | 6.948 | 1.00 | 9.64 |
| ATOM | 287 | O | MET | A | 38 | 14.869 | 6.661 | 6.420 | 1.00 | 9.28 |
| ATOM | 288 | N | PHE | A | 39 | 12.626 | 6.394 | 6.412 | 1.00 | 10.04 |
| ATOM | 289 | CA | PHE | A | 39 | 12.454 | 7.148 | 5.193 | 1.00 | 9.68 |
| ATOM | 290 | CB | PHE | A | 39 | 11.047 | 6.979 | 4.613 | 1.00 | 10.54 |
| ATOM | 291 | CG | PHE | A | 39 | 10.854 | 7.685 | 3.299 | 1.00 | 11.39 |
| ATOM | 292 | CD1 | PHE | A | 39 | 11.103 | 7.027 | 2.094 | 1.00 | 11.41 |
| ATOM | 293 | CD2 | PHE | A | 39 | 10.460 | 9.019 | 3.263 | 1.00 | 12.49 |
| ATOM | 294 | CE1 | PHE | A | 39 | 10.970 | 7.676 | 0.881 | 1.00 | 11.60 |
| ATOM | 295 | CE2 | PHE | A | 39 | 10.321 | 9.689 | 2.049 | 1.00 | 12.07 |
| ATOM | 296 | CZ | PHE | A | 39 | 10.577 | 9.017 | 0.855 | 1.00 | 13.19 |
| ATOM | 297 | C | PHE | A | 39 | 12.754 | 8.623 | 5.468 | 1.00 | 9.58 |
| ATOM | 298 | O | PHE | A | 39 | 13.438 | 9.255 | 4.686 | 1.00 | 12.10 |
| ATOM | 299 | N | ARG | A | 40 | 12.262 | 9.158 | 6.581 | 1.00 | 11.25 |
| ATOM | 300 | CA | ARG | A | 40 | 12.504 | 10.555 | 6.956 | 1.00 | 12.04 |
| ATOM | 301 | CB | ARG | A | 40 | 11.844 | 10.847 | 8.304 | 1.00 | 11.50 |
| ATOM | 302 | CG | ARG | A | 40 | 12.173 | 12.195 | 8.950 | 1.00 | 11.61 |
| ATOM | 303 | CD | ARG | A | 40 | 11.646 | 12.213 | 10.373 | 1.00 | 14.39 |
| ATOM | 304 | NE | ARG | A | 40 | 11.588 | 13.549 | 10.969 | 1.00 | 15.72 |
| ATOM | 305 | CZ | ARG | A | 40 | 11.643 | 13.800 | 12.278 | 1.00 | 16.09 |
| ATOM | 306 | NH1 | ARG | A | 40 | 11.760 | 12.811 | 13.152 | 1.00 | 15.42 |
| ATOM | 307 | NH2 | ARG | A | 40 | 11.558 | 15.050 | 12.723 | 1.00 | 15.62 |
| ATOM | 308 | C | ARG | A | 40 | 14.013 | 10.825 | 7.051 | 1.00 | 13.28 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 309 | O | ARG | A | 40 | 14.485 | 11.912 | 6.723 | 1.00 | 13.32 |
| ATOM | 310 | N | LYS | A | 41 | 14.766 | 9.819 | 7.485 | 1.00 | 14.01 |
| ATOM | 311 | CA | LYS | A | 41 | 16.211 | 9.929 | 7.624 | 1.00 | 13.57 |
| ATOM | 312 | CB | LYS | A | 41 | 16.692 | 8.939 | 8.677 | 1.00 | 13.59 |
| ATOM | 313 | CG | LYS | A | 41 | 18.199 | 8.909 | 8.844 | 1.00 | 14.72 |
| ATOM | 314 | CD | LYS | A | 41 | 18.644 | 7.794 | 9.782 | 1.00 | 16.77 |
| ATOM | 315 | CE | LYS | A | 41 | 20.126 | 7.831 | 10.058 | 1.00 | 18.29 |
| ATOM | 316 | NZ | LYS | A | 41 | 20.924 | 7.748 | 8.795 | 1.00 | 21.26 |
| ATOM | 317 | C | LYS | A | 41 | 17.029 | 9.725 | 6.339 | 1.00 | 14.01 |
| ATOM | 318 | O | LYS | A | 41 | 17.961 | 10.485 | 6.072 | 1.00 | 15.48 |
| ATOM | 319 | N | THR | A | 42 | 16.676 | 8.717 | 5.542 | 1.00 | 12.25 |
| ATOM | 320 | CA | THR | A | 42 | 17.427 | 8.378 | 4.331 | 1.00 | 10.80 |
| ATOM | 321 | CB | THR | A | 42 | 17.848 | 6.887 | 4.351 | 1.00 | 10.53 |
| ATOM | 322 | OG1 | THR | A | 42 | 16.703 | 6.061 | 4.060 | 1.00 | 9.82 |
| ATOM | 323 | CG2 | THR | A | 42 | 18.411 | 6.510 | 5.717 | 1.00 | 6.89 |
| ATOM | 324 | C | THR | A | 42 | 16.751 | 8.590 | 2.989 | 1.00 | 11.11 |
| ATOM | 325 | O | THR | A | 42 | 17.405 | 8.534 | 1.949 | 1.00 | 12.23 |
| ATOM | 326 | N | GLY | A | 43 | 15.437 | 8.745 | 2.988 | 1.00 | 11.19 |
| ATOM | 327 | CA | GLY | A | 43 | 14.737 | 8.918 | 1.728 | 1.00 | 12.38 |
| ATOM | 328 | C | GLY | A | 43 | 14.509 | 7.612 | 0.977 | 1.00 | 12.46 |
| ATOM | 329 | O | GLY | A | 43 | 14.161 | 7.630 | -0.207 | 1.00 | 12.41 |
| ATOM | 330 | N | ALA | A | 44 | 14.698 | 6.480 | 1.657 | 1.00 | 12.34 |
| ATOM | 331 | CA | ALA | A | 44 | 14.491 | 5.168 | 1.039 | 1.00 | 11.41 |
| ATOM | 332 | CB | ALA | A | 44 | 15.806 | 4.366 | 1.004 | 1.00 | 11.51 |
| ATOM | 333 | C | ALA | A | 44 | 13.428 | 4.419 | 1.830 | 1.00 | 10.15 |
| ATOM | 334 | O | ALA | A | 44 | 13.487 | 4.369 | 3.063 | 1.00 | 10.10 |
| ATOM | 335 | N | LEU | A | 45 | 12.422 | 3.904 | 1.128 | 1.00 | 8.85 |
| ATOM | 336 | CA | LEU | A | 45 | 11.339 | 3.150 | 1.763 | 1.00 | 7.67 |
| ATOM | 337 | CB | LEU | A | 45 | 9.985 | 3.444 | 1.096 | 1.00 | 4.50 |
| ATOM | 338 | CG | LEU | A | 45 | 8.769 | 2.740 | 1.723 | 1.00 | 4.04 |
| ATOM | 339 | CD1 | LEU | A | 45 | 8.539 | 3.204 | 3.165 | 1.00 | 2.51 |
| ATOM | 340 | CD2 | LEU | A | 45 | 7.518 | 2.974 | 0.883 | 1.00 | 3.79 |
| ATOM | 341 | C | LEU | A | 45 | 11.627 | 1.665 | 1.669 | 1.00 | 6.73 |
| ATOM | 342 | O | LEU | A | 45 | 11.572 | 1.096 | 0.592 | 1.00 | 7.76 |
| ATOM | 343 | N | ILE | A | 46 | 11.974 | 1.044 | 2.796 | 1.00 | 8.21 |
| ATOM | 344 | CA | ILE | A | 46 | 12.255 | -0.395 | 2.817 | 1.00 | 7.41 |
| ATOM | 345 | CB | ILE | A | 46 | 13.728 | -0.700 | 3.237 | 1.00 | 7.58 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 346 | CG2 | ILE | A | 46 | 14.013 | -2.222 | 3.131 | 1.00 | 8.78 |
| ATOM | 347 | CG1 | ILE | A | 46 | 14.715 | 0.089 | 2.367 | 1.00 | 9.49 |
| ATOM | 348 | CD1 | ILE | A | 46 | 16.173 | -0.074 | 2.783 | 1.00 | 10.00 |
| ATOM | 349 | C | ILE | A | 46 | 11.301 | -1.116 | 3.783 | 1.00 | 6.16 |
| ATOM | 350 | O | ILE | A | 46 | 11.241 | -0.786 | 4.968 | 1.00 | 6.62 |
| ATOM | 351 | N | SER | A | 47 | 10.546 | -2.085 | 3.273 | 1.00 | 5.59 |
| ATOM | 352 | CA | SER | A | 47 | 9.630 | -2.847 | 4.114 | 1.00 | 6.27 |
| ATOM | 353 | CB | SER | A | 47 | 8.764 | -3.767 | 3.253 | 1.00 | 5.22 |
| ATOM | 354 | OG | SER | A | 47 | 7.738 | -4.356 | 4.021 | 1.00 | 7.41 |
| ATOM | 355 | C | SER | A | 47 | 10.451 | -3.636 | 5.157 | 1.00 | 5.90 |
| ATOM | 356 | O | SER | A | 47 | 11.492 | -4.234 | 4.835 | 1.00 | 4.59 |
| ATOM | 357 | N | LEU | A | 48 | 10.019 | -3.574 | 6.417 | 1.00 | 5.25 |
| ATOM | 358 | CA | LEU | A | 48 | 10.717 | -4.226 | 7.529 | 1.00 | 5.28 |
| ATOM | 359 | CB | LEU | A | 48 | 10.895 | -3.229 | 8.685 | 1.00 | 4.88 |
| ATOM | 360 | CG | LEU | A | 48 | 11.595 | -1.897 | 8.317 | 1.00 | 5.79 |
| ATOM | 361 | CD1 | LEU | A | 48 | 11.445 | -0.883 | 9.440 | 1.00 | 3.48 |
| ATOM | 362 | CD2 | LEU | A | 48 | 13.075 | -2.129 | 8.009 | 1.00 | 4.77 |
| ATOM | 363 | C | LEU | A | 48 | 10.045 | -5.506 | 8.022 | 1.00 | 5.07 |
| ATOM | 364 | O | LEU | A | 48 | 8.834 | -5.682 | 7.906 | 1.00 | 4.73 |
| ATOM | 365 | N | SER | A | 49 | 10.836 | -6.355 | 8.660 | 1.00 | 5.94 |
| ATOM | 366 | CA | SER | A | 49 | 10.382 | -7.651 | 9.155 | 1.00 | 4.45 |
| ATOM | 367 | CB | SER | A | 49 | 11.588 | -8.592 | 9.250 | 1.00 | 6.13 |
| ATOM | 368 | OG | SER | A | 49 | 11.220 | -9.886 | 9.690 | 1.00 | 8.26 |
| ATOM | 369 | C | SER | A | 49 | 9.580 | -7.714 | 10.448 | 1.00 | 2.44 |
| ATOM | 370 | O | SER | A | 49 | 10.111 | -7.541 | 11.551 | 1.00 | 2.00 |
| ATOM | 371 | N | GLU | A | 50 | 8.283 | -7.959 | 10.313 | 1.00 | 2.00 |
| ATOM | 372 | CA | GLU | A | 50 | 7.446 | -8.114 | 11.489 | 1.00 | 3.02 |
| ATOM | 373 | CB | GLU | A | 50 | 5.962 | -8.130 | 11.120 | 1.00 | 4.09 |
| ATOM | 374 | CG | GLU | A | 50 | 5.408 | -6.788 | 10.663 | 1.00 | 2.50 |
| ATOM | 375 | CD | GLU | A | 50 | 5.660 | -6.518 | 9.199 | 1.00 | 5.11 |
| ATOM | 376 | OE1 | GLU | A | 50 | 5.945 | -7.463 | 8.448 | 1.00 | 7.22 |
| ATOM | 377 | OE2 | GLU | A | 50 | 5.553 | -5.360 | 8.774 | 1.00 | 7.90 |
| ATOM | 378 | C | GLU | A | 50 | 7.815 | -9.451 | 12.126 | 1.00 | 2.00 |
| ATOM | 379 | O | GLU | A | 50 | 7.712 | -9.606 | 13.322 | 1.00 | 3.82 |
| ATOM | 380 | N | GLN | A | 51 | 8.251 | -10.410 | 11.313 | 1.00 | 4.25 |
| ATOM | 381 | CA | GLN | A | 51 | 8.622 | -11.731 | 11.818 | 1.00 | 3.90 |
| ATOM | 382 | CB | GLN | A | 51 | 8.869 | -12.704 | 10.668 | 1.00 | 2.10 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 383 | CG | GLN | A | 51 | 8.780 | -14.206 | 11.068 | 1.00 | 2.85 |
| ATOM | 384 | CD | GLN | A | 51 | 7.434 | -14.576 | 11.684 | 1.00 | 2.00 |
| ATOM | 385 | OE1 | GLN | A | 51 | 6.389 | -14.312 | 11.112 | 1.00 | 2.00 |
| ATOM | 386 | NE2 | GLN | A | 51 | 7.464 | -15.193 | 12.852 | 1.00 | 2.68 |
| ATOM | 387 | C | GLN | A | 51 | 9.845 | -11.628 | 12.735 | 1.00 | 3.62 |
| ATOM | 388 | O | GLN | A | 51 | 9.873 | -12.277 | 13.788 | 1.00 | 2.53 |
| ATOM | 389 | N | ASP | A | 52 | 10.794 | -10.747 | 12.373 | 1.00 | 3.63 |
| ATOM | 390 | CA | ASP | A | 52 | 11.994 | -10.491 | 13.161 | 1.00 | 2.57 |
| ATOM | 391 | CB | ASP | A | 52 | 12.835 | -9.375 | 12.517 | 1.00 | -3.71 |
| ATOM | 392 | CG | ASP | A | 52 | 14.259 | -9.262 | 13.098 | 1.00 | 2.59 |
| ATOM | 393 | OD1 | ASP | A | 52 | 14.531 | -9.695 | 14.234 | 1.00 | 3.36 |
| ATOM | 394 | OD2 | ASP | A | 52 | 15.128 | -8.711 | 12.399 | 1.00 | 2.44 |
| ATOM | 395 | C | ASP | A | 52 | 11.565 | -10.083 | 14.567 | 1.00 | 4.37 |
| ATOM | 396 | O | ASP | A | 52 | 12.081 | -10.608 | 15.563 | 1.00 | 3.75 |
| ATOM | 397 | N | LEU | A | 53 | 10.607 | -9.158 | 14.641 | 1.00 | 2.86 |
| ATOM | 398 | CA | LEU | A | 53 | 10.072 | -8.675 | 15.915 | 1.00 | 2.00 |
| ATOM | 399 | CB | LEU | A | 53 | 9.085 | -7.532 | 15.658 | 1.00 | 2.60 |
| ATOM | 400 | CG | LEU | A | 53 | 9.652 | -6.204 | 15.164 | 1.00 | 2.67 |
| ATOM | 401 | CD1 | LEU | A | 53 | 8.493 | -5.237 | 14.963 | 1.00 | 2.00 |
| ATOM | 402 | CD2 | LEU | A | 53 | 10.675 | -5.655 | 16.189 | 1.00 | 2.00 |
| ATOM | 403 | C | LEU | A | 53 | 9.361 | -9.768 | 16.729 | 1.00 | 2.00 |
| ATOM | 404 | O | LEU | A | 53 | 9.631 | -9.943 | 17.931 | 1.00 | 2.00 |
| ATOM | 405 | N | VAL | A | 54 | 8.421 | -10.458 | 16.073 | 1.00 | 3.82 |
| ATOM | 406 | CA | VAL | A | 54 | 7.619 | -11.533 | 16.681 | 1.00 | 4.97 |
| ATOM | 407 | CB | VAL | A | 54 | 6.610 | -12.172 | 15.592 | 1.00 | 4.86 |
| ATOM | 408 | CG1 | VAL | A | 54 | 5.887 | -13.410 | 16.124 | 1.00 | 3.66 |
| ATOM | 409 | CG2 | VAL | A | 54 | 5.543 | -11.155 | 15.186 | 1.00 | 4.34 |
| ATOM | 410 | C | VAL | A | 54 | 8.519 | -12.603 | 17.342 | 1.00 | 4.50 |
| ATOM | 411 | O | VAL | A | 54 | 8.348 | -12.928 | 18.509 | 1.00 | 5.80 |
| ATOM | 412 | N | ASP | A | 55 | 9.545 | -13.040 | 16.616 | 1.00 | 6.09 |
| ATOM | 413 | CA | ASP | A | 55 | 10.476 | -14.079 | 17.064 | 1.00 | 4.92 |
| ATOM | 414 | CB | ASP | A | 55 | 11.230 | -14.674 | 15.860 | 1.00 | 3.20 |
| ATOM | 415 | CG | ASP | A | 55 | 10.337 | -15.304 | 14.818 | 1.00 | 3.85 |
| ATOM | 416 | OD1 | ASP | A | 55 | 9.150 | -15.595 | 15.091 | 1.00 | 4.72 |
| ATOM | 417 | OD2 | ASP | A | 55 | 10.857 | -15.536 | 13.703 | 1.00 | 2.72 |
| ATOM | 418 | C | ASP | A | 55 | 11.580 | -13.641 | 18.014 | 1.00 | 6.95 |
| ATOM | 419 | O | ASP | A | 55 | 12.158 | -14.469 | 18.720 | 1.00 | 7.17 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 420 | N | CYS | A | 56 | 11.952 | -12.366 | 17.975 | 1.00 | 8.58 |
| ATOM | 421 | CA | CYS | A | 56 | 13.084 | -11.938 | 18.776 | 1.00 | 6.99 |
| ATOM | 422 | C | CYS | A | 56 | 12.895 | -10.988 | 19.927 | 1.00 | 7.01 |
| ATOM | 423 | O | CYS | A | 56 | 13.787 | -10.883 | 20.769 | 1.00 | 10.34 |
| ATOM | 424 | CB | CYS | A | 56 | 14.137 | -11.350 | 17.847 | 1.00 | 5.98 |
| ATOM | 425 | SG | CYS | A | 56 | 14.501 | -12.313 | 16.357 | 1.00 | 6.00 |
| ATOM | 426 | N | SER | A | 57 | 11.779 | -10.278 | 19.987 | 1.00 | 9.08 |
| ATOM | 427 | CA | SER | A | 57 | 11.612 | -9.303 | 21.068 | 1.00 | 10.69 |
| ATOM | 428 | CB | SER | A | 57 | 10.918 | -8.034 | 20.568 | 1.00 | 8.58 |
| ATOM | 429 | OG | SER | A | 57 | 9.566 | -8.285 | 20.294 | 1.00 | 9.77 |
| ATOM | 430 | C | SER | A | 57 | 10.988 | -9.781 | 22.372 | 1.00 | 11.68 |
| ATOM | 431 | O | SER | A | 57 | 10.432 | -8.993 | 23.134 | 1.00 | 12.62 |
| ATOM | 432 | N | GLY | A | 58 | 11.121 | -11.071 | 22.651 | 1.00 | 13.83 |
| ATOM | 433 | CA | GLY | A | 58 | 10.610 | -11.608 | 23.895 | 1.00 | 11.63 |
| ATOM | 434 | C | GLY | A | 58 | 11.292 | -10.972 | 25.093 | 1.00 | 11.54 |
| ATOM | 435 | O | GLY | A | 58 | 10.626 | -10.642 | 26.071 | 1.00 | 11.23 |
| ATOM | 436 | N | PRO | A | 59 | 12.611 | -10.727 | 25.041 | 1.00 | 12.29 |
| ATOM | 437 | CD | PRO | A | 59 | 13.594 | -11.044 | 23.993 | 1.00 | 11.81 |
| ATOM | 438 | CA | PRO | A | 59 | 13.272 | -10.115 | 26.199 | 1.00 | 11.93 |
| ATOM | 439 | CB | PRO | A | 59 | 14.719 | -9.992 | 25.728 | 1.00 | 13.40 |
| ATOM | 440 | CG | PRO | A | 59 | 14.869 | -11.106 | 24.763 | 1.00 | 12.49 |
| ATOM | 441 | C | PRO | A | 59 | 12.702 | -8.735 | 26.584 | 1.00 | 12.46 |
| ATOM | 442 | O | PRO | A | 59 | 12.724 | -8.346 | 27.758 | 1.00 | 12.90 |
| ATOM | 443 | N | GLN | A | 60 | 12.163 | -8.020 | 25.601 | 1.00 | 10.55 |
| ATOM | 444 | CA | GLN | A | 60 | 11.605 | -6.691 | 25.830 | 1.00 | 8.86 |
| ATOM | 445 | CB | GLN | A | 60 | 11.714 | -5.849 | 24.540 | 1.00 | 7.26 |
| ATOM | 446 | CG | GLN | A | 60 | 13.155 | -5.391 | 24.210 | 1.00 | 6.32 |
| ATOM | 447 | CD | GLN | A | 60 | 14.102 | -6.498 | 23.724 | 1.00 | 6.43 |
| ATOM | 448 | OE1 | GLN | A | 60 | 15.333 | -6.364 | 23.797 | 1.00 | 7.70 |
| ATOM | 449 | NE2 | GLN | A | 60 | 13.543 | -7.546 | 23.158 | 1.00 | 3.38 |
| ATOM | 450 | C | GLN | A | 60 | 10.183 | -6.676 | 26.410 | 1.00 | 7.36 |
| ATOM | 451 | O | GLN | A | 60 | 9.701 | -5.630 | 26.821 | 1.00 | 6.68 |
| ATOM | 452 | N | GLY | A | 61 | 9.544 | -7.844 | 26.483 | 1.00 | 5.53 |
| ATOM | 453 | CA | GLY | A | 61 | 8.209 | -7.933 | 27.032 | 1.00 | 5.09 |
| ATOM | 454 | C | GLY | A | 61 | 7.161 | -8.339 | 26.015 | 1.00 | 7.10 |
| ATOM | 455 | O | GLY | A | 61 | 5.963 | -8.385 | 26.320 | 1.00 | 9.01 |
| ATOM | 456 | N | ASN | A | 62 | 7.588 | -8.551 | 24.776 | 1.00 | 7.60 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 457 | CA | ASN | A | 62 | 6.654 | -8.953 | 23.725 | 1.00 | 9.01 |
| ATOM | 458 | CB | ASN | A | 62 | 7.146 | -8.537 | 22.331 | 1.00 | 6.76 |
| ATOM | 459 | CG | ASN | A | 62 | 7.023 | -7.033 | 22.092 | 1.00 | 6.05 |
| ATOM | 460 | OD1 | ASN | A | 62 | 7.785 | -6.436 | 21.334 | 1.00 | 5.37 |
| ATOM | 461 | ND2 | ASN | A | 62 | 6.059 | -6.421 | 22.741 | 1.00 | 3.19 |
| ATOM | 462 | C | ASN | A | 62 | 6.431 | -10.447 | 23.807 | 1.00 | 9.14 |
| ATOM | 463 | O | ASN | A | 62 | 7.328 | -11.196 | 24.198 | 1.00 | 9.09 |
| ATOM | 464 | N | GLU | A | 63 | 5.213 | -10.867 | 23.500 | 1.00 | 10.86 |
| ATOM | 465 | CA | GLU | A | 63 | 4.867 | -12.273 | 23.555 | 1.00 | 11.00 |
| ATOM | 466 | CB | GLU | A | 63 | 3.867 | -12.509 | 24.679 | 1.00 | 11.80 |
| ATOM | 467 | CG | GLU | A | 63 | 4.503 | -12.259 | 26.052 | 1.00 | 13.06 |
| ATOM | 468 | CD | GLU | A | 63 | 3.661 | -12.738 | 27.209 | 1.00 | 14.45 |
| ATOM | 469 | OE1 | GLU | A | 63 | 2.832 | -13.650 | 27.026 | 1.00 | 18.29 |
| ATOM | 470 | OE2 | GLU | A | 63 | 3.826 | -12.193 | 28.313 | 1.00 | 15.14 |
| ATOM | 471 | C | GLU | A | 63 | 4.423 | -12.886 | 22.233 | 1.00 | 10.77 |
| ATOM | 472 | O | GLU | A | 63 | 3.382 | -13.546 | 22.147 | 1.00 | 11.14 |
| ATOM | 473 | N | GLY | A | 64 | 5.250 | -12.678 | 21.211 | 1.00 | 10.35 |
| ATOM | 474 | CA | GLY | A | 64 | 4.993 | -13.223 | 19.887 | 1.00 | 10.93 |
| ATOM | 475 | C | GLY | A | 64 | 3.616 | -13.023 | 19.304 | 1.00 | 11.79 |
| ATOM | 476 | O | GLY | A | 64 | 3.197 | -11.888 | 19.077 | 1.00 | 11.98 |
| ATOM | 477 | N | CYS | A | 65 | 2.907 | -14.121 | 19.034 | 1.00 | 11.17 |
| ATOM | 478 | CA | CYS | A | 65 | 1.571 | -14.022 | 18.454 | 1.00 | 10.14 |
| ATOM | 479 | C | CYS | A | 65 | 0.468 | -13.822 | 19.469 | 1.00 | 10.16 |
| ATOM | 480 | O | CYS | A | 65 | -0.704 | -13.808 | 19.110 | 1.00 | 11.53 |
| ATOM | 481 | CB | CYS | A | 65 | 1.230 | -15.234 | 17.572 | 1.00 | 9.54 |
| ATOM | 482 | SG | CYS | A | 65 | 2.067 | -15.291 | 15.961 | 1.00 | 10.24 |
| ATOM | 483 | N | ASN | A | 66 | 0.823 | -13.697 | 20.734 | 1.00 | 12.32 |
| ATOM | 484 | CA | ASN | A | 66 | -0.187 | -13.482 | 21.764 | 1.00 | 14.74 |
| ATOM | 485 | CB | ASN | A | 66 | 0.075 | -14.386 | 22.956 | 1.00 | 15.93 |
| ATOM | 486 | CG | ASN | A | 66 | -0.198 | -15.818 | 22.635 | 1.00 | 17.25 |
| ATOM | 487 | OD1 | ASN | A | 66 | 0.724 | -16.637 | 22.569 | 1.00 | 19.52 |
| ATOM | 488 | ND2 | ASN | A | 66 | -1.459 | -16.129 | 22.362 | 1.00 | 15.97 |
| ATOM | 489 | C | ASN | A | 66 | -0.319 | -12.032 | 22.218 | 1.00 | 14.67 |
| ATOM | 490 | O | ASN | A | 66 | -1.215 | -11.700 | 23.016 | 1.00 | 15.81 |
| ATOM | 491 | N | GLY | A | 67 | 0.563 | -11.178 | 21.695 | 1.00 | 13.07 |
| ATOM | 492 | CA | GLY | A | 67 | 0.530 | -9.766 | 22.036 | 1.00 | 11.36 |
| ATOM | 493 | C | GLY | A | 67 | 1.890 | -9.134 | 22.235 | 1.00 | 8.74 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 494 | O | GLY | A | 67 | 2.909 | -9.825 | 22.326 | 1.00 | 8.51 |
| ATOM | 495 | N | GLY | A | 68 | 1.887 | -7.807 | 22.328 | 1.00 | 7.52 |
| ATOM | 496 | CA | GLY | A | 68 | 3.105 | -7.041 | 22.514 | 1.00 | 7.10 |
| ATOM | 497 | C | GLY | A | 68 | 2.805 | -5.555 | 22.423 | 1.00 | 6.68 |
| ATOM | 498 | O | GLY | A | 68 | 1.672 | -5.177 | 22.161 | 1.00 | 7.62 |
| ATOM | 499 | N | LEU | A | 69 | 3.814 | -4.718 | 22.640 | 1.00 | 7.01 |
| ATOM | 500 | CA | LEU | A | 69 | 3.659 | -3.264 | 22.586 | 1.00 | 5.71 |
| ATOM | 501 | CB | LEU | A | 69 | 3.891 | -2.631 | 23.955 | 1.00 | 7.16 |
| ATOM | 502 | CG | LEU | A | 69 | 3.055 | -3.047 | 25.166 | 1.00 | 9.21 |
| ATOM | 503 | CD1 | LEU | A | 69 | 3.509 | -2.219 | 26.375 | 1.00 | 10.10 |
| ATOM | 504 | CD2 | LEU | A | 69 | 1.567 | -2.864 | 24.906 | 1.00 | 8.93 |
| ATOM | 505 | C | LEU | A | 69 | 4.658 | -2.678 | 21.607 | 1.00 | 5.71 |
| ATOM | 506 | O | LEU | A | 69 | 5.781 | -3.147 | 21.491 | 1.00 | 4.13 |
| ATOM | 507 | N | MET | A | 70 | 4.237 | -1.646 | 20.895 | 1.00 | 5.70 |
| ATOM | 508 | CA | MET | A | 70 | 5.098 | -0.982 | 19.926 | 1.00 | 5.04 |
| ATOM | 509 | CB | MET | A | 70 | 4.334 | 0.146 | 19.214 | 1.00 | 3.69 |
| ATOM | 510 | CG | MET | A | 70 | 3.213 | -0.342 | 18.286 | 1.00 | 2.10 |
| ATOM | 511 | SD | MET | A | 70 | 1.712 | -0.933 | 19.131 | 1.00 | 2.01 |
| ATOM | 512 | CE | MET | A | 70 | 0.824 | 0.573 | 19.277 | 1.00 | 2.00 |
| ATOM | 513 | C | MET | A | 70 | 6.364 | -0.452 | 20.569 | 1.00 | 3.03 |
| ATOM | 514 | O | MET | A | 70 | 7.440 | -0.549 | 19.990 | 1.00 | 4.19 |
| ATOM | 515 | N | ASP | A | 71 | 6.249 | 0.064 | 21.787 | 1.00 | 3.16 |
| ATOM | 516 | CA | ASP | A | 71 | 7.422 | 0.575 | 22.479 | 1.00 | 2.25 |
| ATOM | 517 | CB | ASP | A | 71 | 7.029 | 1.307 | 23.740 | 1.00 | 2.00 |
| ATOM | 518 | CG | ASP | A | 71 | 6.437 | 2.646 | 23.443 | 1.00 | 2.00 |
| ATOM | 519 | OD1 | ASP | A | 71 | 6.532 | 3.094 | 22.281 | 1.00 | 2.00 |
| ATOM | 520 | OD2 | ASP | A | 71 | 5.859 | 3.236 | 24.359 | 1.00 | 3.76 |
| ATOM | 521 | C | ASP | A | 71 | 8.416 | -0.510 | 22.778 | 1.00 | 3.38 |
| ATOM | 522 | O | ASP | A | 71 | 9.615 | -0.282 | 22.658 | 1.00 | 2.40 |
| ATOM | 523 | N | TYR | A | 72 | 7.917 | -1.698 | 23.115 | 1.00 | 2.72 |
| ATOM | 524 | CA | TYR | A | 72 | 8.790 | -2.842 | 23.396 | 1.00 | 3.10 |
| ATOM | 525 | CB | TYR | A | 72 | 7.978 | -4.052 | 23.878 | 1.00 | 3.23 |
| ATOM | 526 | CG | TYR | A | 72 | 7.390 | -3.950 | 25.271 | 1.00 | 2.49 |
| ATOM | 527 | CD1 | TYR | A | 72 | 7.770 | -2.939 | 26.145 | 1.00 | 4.46 |
| ATOM | 528 | CE1 | TYR | A | 72 | 7.236 | -2.859 | 27.418 | 1.00 | 4.52 |
| ATOM | 529 | CD2 | TYR | A | 72 | 6.457 | -4.884 | 25.714 | 1.00 | 2.65 |
| ATOM | 530 | CE2 | TYR | A | 72 | 5.916 | -4.818 | 26.983 | 1.00 | 3.69 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 531 | CZ | TYR | A | 72 | 6.308 | -3.807 | 27.821 | 1.00 | 5.94 |
| ATOM | 532 | OH | TYR | A | 72 | 5.749 | -3.723 | 29.054 | 1.00 | 8.70 |
| ATOM | 533 | C | TYR | A | 72 | 9.550 | -3.231 | 22.128 | 1.00 | 2.21 |
| ATOM | 534 | O | TYR | A | 72 | 10.666 | -3.728 | 22.198 | 1.00 | 4.44 |
| ATOM | 535 | N | ALA | A | 73 | 8.925 | -3.025 | 20.971 | 1.00 | 2.81 |
| ATOM | 536 | CA | ALA | A | 73 | 9.527 | -3.328 | 19.680 | 1.00 | 2.00 |
| ATOM | 537 | CB | ALA | A | 73 | 8.456 | -3.359 | 18.600 | 1.00 | 4.15 |
| ATOM | 538 | C | ALA | A | 73 | 10.597 | -2.317 | 19.322 | 1.00 | 2.44 |
| ATOM | 539 | O | ALA | A | 73 | 11.615 | -2.663 | 18.739 | 1.00 | 2.00 |
| ATOM | 540 | N | PHE | A | 74 | 10.332 | -1.045 | 19.615 | 1.00 | 3.81 |
| ATOM | 541 | CA | PHE | A | 74 | 11.306 | 0.027 | 19.368 | 1.00 | 4.29 |
| ATOM | 542 | CB | PHE | A | 74 | 10.662 | 1.396 | 19.614 | 1.00 | 2.00 |
| ATOM | 543 | CG | PHE | A | 74 | 9.516 | 1.700 | 18.690 | 1.00 | 2.00 |
| ATOM | 544 | CD1 | PHE | A | 74 | 8.407 | 2.407 | 19.150 | 1.00 | 2.28 |
| ATOM | 545 | CD2 | PHE | A | 74 | 9.520 | 1.244 | 17.377 | 1.00 | 2.00 |
| ATOM | 546 | CE1 | PHE | A | 74 | 7.315 | 2.650 | 18.317 | 1.00 | 2.00 |
| ATOM | 547 | CE2 | PHE | A | 74 | 8.428 | 1.483 | 16.529 | 1.00 | 2.97 |
| ATOM | 548 | CZ | PHE | A | 74 | 7.325 | 2.189 | 17.012 | 1.00 | 2.00 |
| ATOM | 549 | C | PHE | A | 74 | 12.530 | -0.200 | 20.285 | 1.00 | 2.69 |
| ATOM | 550 | O | PHE | A | 74 | 13.678 | -0.007 | 19.873 | 1.00 | 4.23 |
| ATOM | 551 | N | GLN | A | 75 | 12.281 | -0.631 | 21.521 | 1.00 | 3.82 |
| ATOM | 552 | CA | GLN | A | 75 | 13.365 | -0.944 | 22.457 | 1.00 | 5.85 |
| ATOM | 553 | CB | GLN | A | 75 | 12.833 | -1.253 | 23.854 | 1.00 | 8.10 |
| ATOM | 554 | CG | GLN | A | 75 | 13.956 | -1.448 | 24.888 | 1.00 | 11.09 |
| ATOM | 555 | CD | GLN | A | 75 | 14.762 | -0.182 | 25.129 | 1.00 | 12.81 |
| ATOM | 556 | OE1 | GLN | A | 75 | 16.003 | -0.168 | 25.067 | 1.00 | 12.82 |
| ATOM | 557 | NE2 | GLN | A | 75 | 14.053 | 0.897 | 25.398 | 1.00 | 15.11 |
| ATOM | 558 | C | GLN | A | 75 | 14.216 | -2.131 | 21.937 | 1.00 | 5.66 |
| ATOM | 559 | O | GLN | A | 75 | 15.437 | -2.119 | 22.075 | 1.00 | 2.44 |
| ATOM | 560 | N | TYR | A | 76 | 13.568 | -3.142 | 21.343 | 1.00 | 5.05 |
| ATOM | 561 | CA | TYR | A | 76 | 14.276 | -4.299 | 20.751 | 1.00 | 4.41 |
| ATOM | 562 | CB | TYR | A | 76 | 13.281 | -5.349 | 20.214 | 1.00 | 2.00 |
| ATOM | 563 | CG | TYR | A | 76 | 13.930 | -6.360 | 19.274 | 1.00 | 2.07 |
| ATOM | 564 | CD1 | TYR | A | 76 | 14.728 | -7.387 | 19.768 | 1.00 | 2.47 |
| ATOM | 565 | CE1 | TYR | A | 76 | 15.394 | -8.253 | 18.912 | 1.00 | 2.00 |
| ATOM | 566 | CD2 | TYR | A | 76 | 13.805 | -6.230 | 17.892 | 1.00 | 2.00 |
| ATOM | 567 | CE2 | TYR | A | 76 | 14.465 | -7.085 | 17.022 | 1.00 | 2.22 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 568 | CZ | TYR | A | 76 | 15.264 | -8.094 | 17.548 | 1.00 | 2.41 |
| ATOM | 569 | OH | TYR | A | 76 | 15.977 | -8.919 | 16.714 | 1.00 | 3.62 |
| ATOM | 570 | C | TYR | A | 76 | 15.212 | -3.884 | 19.605 | 1.00 | 4.56 |
| ATOM | 571 | O | TYR | A | 76 | 16.347 | -4.353 | 19.512 | 1.00 | 5.52 |
| ATOM | 572 | N | VAL | A | 77 | 14.702 | -3.076 | 18.683 | 1.00 | 4.67 |
| ATOM | 573 | CA | VAL | A | 77 | 15.498 | -2.625 | 17.565 | 1.00 | 4.35 |
| ATOM | 574 | CB | VAL | A | 77 | 14.697 | -1.696 | 16.610 | 1.00 | 3.33 |
| ATOM | 575 | CG1 | VAL | A | 77 | 15.581 | -1.252 | 15.443 | 1.00 | 2.00 |
| ATOM | 576 | CG2 | VAL | A | 77 | 13.484 | -2.421 | 16.081 | 1.00 | 3.86 |
| ATOM | 577 | C | VAL | A | 77 | 16.732 | -1.934 | 18.116 | 1.00 | 5.20 |
| ATOM | 578 | O | VAL | A | 77 | 17.836 | -2.200 | 17.668 | 1.00 | 7.18 |
| ATOM | 579 | N | GLN | A | 78 | 16.545 | -1.112 | 19.147 | 1.00 | 7.90 |
| ATOM | 580 | CA | GLN | A | 78 | 17.647 | -0.400 | 19.796 | 1.00 | 8.36 |
| ATOM | 581 | CB | GLN | A | 78 | 17.104 | 0.626 | 20.785 | 1.00 | 7.00 |
| ATOM | 582 | CG | GLN | A | 78 | 18.147 | 1.295 | 21.662 | 1.00 | 7.62 |
| ATOM | 583 | CD | GLN | A | 78 | 17.533 | 2.287 | 22.608 | 1.00 | 7.33 |
| ATOM | 584 | OE1 | GLN | A | 78 | 16.347 | 2.220 | 22.914 | 1.00 | 12.26 |
| ATOM | 585 | NE2 | GLN | A | 78 | 18.328 | 3.218 | 23.072 | 1.00 | 9.76 |
| ATOM | 586 | C | GLN | A | 78 | 18.635 | -1.349 | 20.506 | 1.00 | 9.63 |
| ATOM | 587 | O | GLN | A | 78 | 19.841 | -1.271 | 20.253 | 1.00 | 9.65 |
| ATOM | 588 | N | ASP | A | 79 | 18.138 | -2.213 | 21.400 | 1.00 | 8.44 |
| ATOM | 589 | CA | ASP | A | 79 | 18.994 | -3.177 | 22.115 | 1.00 | 8.37 |
| ATOM | 590 | CB | ASP | A | 79 | 18.160 | -4.051 | 23.060 | 1.00 | 8.46 |
| ATOM | 591 | CG | ASP | A | 79 | 17.514 | -3.270 | 24.188 | 1.00 | 8.10 |
| ATOM | 592 | OD1 | ASP | A | 79 | 17.933 | -2.133 | 24.478 | 1.00 | 10.57 |
| ATOM | 593 | OD2 | ASP | A | 79 | 16.588 | -3.814 | 24.812 | 1.00 | 8.80 |
| ATOM | 594 | C | ASP | A | 79 | 19.745 | -4.093 | 21.148 | 1.00 | 7.97 |
| ATOM | 595 | O | ASP | A | 79 | 20.932 | -4.375 | 21.329 | 1.00 | 6.78 |
| ATOM | 596 | N | ASN | A | 80 | 19.041 | -4.498 | 20.089 | 1.00 | 8.48 |
| ATOM | 597 | CA | ASN | A | 80 | 19.539 | -5.396 | 19.041 | 1.00 | 5.82 |
| ATOM | 598 | CB | ASN | A | 80 | 18.338 | -5.974 | 18.272 | 1.00 | 4.43 |
| ATOM | 599 | CG | ASN | A | 80 | 18.725 | -7.085 | 17.345 | 1.00 | 3.01 |
| ATOM | 600 | OD1 | ASN | A | 80 | 18.482 | -7.028 | 16.139 | 1.00 | 4.09 |
| ATOM | 601 | ND2 | ASN | A | 80 | 19.337 | -8.107 | 17.899 | 1.00 | 2.84 |
| ATOM | 602 | C | ASN | A | 80 | 20.523 | -4.770 | 18.054 | 1.00 | 4.96 |
| ATOM | 603 | O | ASN | A | 80 | 21.316 | -5.469 | 17.425 | 1.00 | 5.58 |
| ATOM | 604 | N | GLY | A | 81 | 20.416 | -3.457 | 17.875 | 1.00 | 5.05 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 605 | CA | GLY | A | 81 | 21.287 | -2.755 | 16.969 | 1.00 | 2.00 |
| ATOM | 606 | C | GLY | A | 81 | 20.883 | -2.967 | 15.539 | 1.00 | 2.53 |
| ATOM | 607 | O | GLY | A | 81 | 21.726 | -2.876 | 14.642 | 1.00 | 2.18 |
| ATOM | 608 | N | GLY | A | 82 | 19.609 | -3.278 | 15.308 | 1.00 | 2.00 |
| ATOM | 609 | CA | GLY | A | 82 | 19.163 | -3.494 | 13.946 | 1.00 | 2.74 |
| ATOM | 610 | C | GLY | A | 82 | 17.855 | -4.243 | 13.852 | 1.00 | 3.52 |
| ATOM | 611 | O | GLY | A | 82 | 17.306 | -4.685 | 14.879 | 1.00 | 3.74 |
| ATOM | 612 | N | ILE | A | 83 | 17.375 | -4.389 | 12.616 | 1.00 | 2.73 |
| ATOM | 613 | CA | ILE | A | 83 | 16.120 | -5.076 | 12.295 | 1.00 | 6.15 |
| ATOM | 614 | CB | ILE | A | 83 | 14.854 | -4.145 | 12.584 | 1.00 | 6.32 |
| ATOM | 615 | CG2 | ILE | A | 83 | 14.908 | -2.893 | 11.784 | 1.00 | 9.06 |
| ATOM | 616 | CG1 | ILE | A | 83 | 13.523 | -4.879 | 12.374 | 1.00 | 6.49 |
| ATOM | 617 | CD1 | ILE | A | 83 | 13.176 | -5.771 | 13.522 | 1.00 | 5.60 |
| ATOM | 618 | C | ILE | A | 83 | 16.241 | -5.441 | 10.819 | 1.00 | 5.04 |
| ATOM | 619 | O | ILE | A | 83 | 16.659 | -4.612 | 10.028 | 1.00 | 6.44 |
| ATOM | 620 | N | ASP | A | 84 | 15.964 | -6.702 | 10.463 | 1.00 | 5.67 |
| ATOM | 621 | CA | ASP | A | 84 | 16.081 | -7.152 | 9.072 | 1.00 | 5.79 |
| ATOM | 622 | CB | ASP | A | 84 | 16.131 | -8.690 | 8.965 | 1.00 | 6.39 |
| ATOM | 623 | CG | ASP | A | 84 | 17.361 | -9.291 | 9.626 | 1.00 | 7.46 |
| ATOM | 624 | OD1 | ASP | A | 84 | 18.440 | -8.668 | 9.610 | 1.00 | 8.44 |
| ATOM | 625 | OD2 | ASP | A | 84 | 17.259 | -10.407 | 10.167 | 1.00 | 7.67 |
| ATOM | 626 | C | ASP | A | 84 | 14.949 | -6.653 | 8.223 | 1.00 | 6.09 |
| ATOM | 627 | O | ASP | A | 84 | 13.901 | -6.238 | 8.731 | 1.00 | 7.75 |
| ATOM | 628 | N | SER | A | 85 | 15.161 | -6.701 | 6.917 | 1.00 | 6.34 |
| ATOM | 629 | CA | SER | A | 85 | 14.150 | -6.294 | 5.963 | 1.00 | 7.18 |
| ATOM | 630 | CB | SER | A | 85 | 14.800 | -6.046 | 4.598 | 1.00 | 7.55 |
| ATOM | 631 | OG | SER | A | 85 | 15.465 | -7.209 | 4.130 | 1.00 | 9.24 |
| ATOM | 632 | C | SER | A | 85 | 13.057 | -7.370 | 5.838 | 1.00 | 7.67 |
| ATOM | 633 | O | SER | A | 85 | 13.266 | -8.539 | 6.180 | 1.00 | 7.18 |
| ATOM | 634 | N | GLU | A | 86 | 11.884 | -6.952 | 5.380 | 1.00 | 5.49 |
| ATOM | 635 | CA | GLU | A | 86 | 10.763 | -7.838 | 5.173 | 1.00 | 6.04 |
| ATOM | 636 | CB | GLU | A | 86 | 9.578 | -7.046 | 4.600 | 1.00 | 5.74 |
| ATOM | 637 | CG | GLU | A | 86 | 8.282 | -7.847 | 4.425 | 1.00 | 4.00 |
| ATOM | 638 | CD | GLU | A | 86 | 7.547 | -8.038 | 5.714 | 1.00 | 5.24 |
| ATOM | 639 | OE1 | GLU | A | 86 | 6.788 | -7.128 | 6.077 | 1.00 | 6.23 |
| ATOM | 640 | OE2 | GLU | A | 86 | 7.711 | -9.084 | 6.379 | 1.00 | 6.50 |
| ATOM | 641 | C | GLU | A | 86 | 11.199 | -8.919 | 4.173 | 1.00 | 7.54 |

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ATOM    642  O   GLU A  86      10.856 -10.096   4.324  1.00  6.89
ATOM    643  N   GLU A  87      11.952  -8.506   3.156  1.00  9.17
ATOM    644  CA  GLU A  87      12.439  -9.408   2.126  1.00  9.73
ATOM    645  CB  GLU A  87      13.196  -8.630   1.053  1.00 12.02
ATOM    646  CG  GLU A  87      13.623  -9.477  -0.118  1.00 15.12
ATOM    647  CD  GLU A  87      14.459  -8.724  -1.131  1.00 18.16
ATOM    648  OE1 GLU A  87      14.230  -7.516  -1.339  1.00 21.29
ATOM    649  OE2 GLU A  87      15.344  -9.350  -1.740  1.00 19.92
ATOM    650  C   GLU A  87      13.331 -10.519   2.670  1.00  9.79
ATOM    651  O   GLU A  87      13.149 -11.669   2.322  1.00 10.68
ATOM    652  N   SER A  88      14.285 -10.173   3.528  1.00 10.39
ATOM    653  CA  SER A  88      15.218 -11.156   4.093  1.00  9.48
ATOM    654  CB  SER A  88      16.469 -10.443   4.640  1.00  8.86
ATOM    655  OG  SER A  88      16.239  -9.825   5.907  1.00  7.26
ATOM    656  C   SER A  88      14.643 -12.051   5.196  1.00  8.73
ATOM    657  O   SER A  88      15.146 -13.151   5.430  1.00  7.49
ATOM    658  N   TYR A  89      13.590 -11.576   5.858  1.00  7.24
ATOM    659  CA  TYR A  89      12.978 -12.275   6.983  1.00  6.63
ATOM    660  CB  TYR A  89      13.493 -11.594   8.255  1.00  3.81
ATOM    661  CG  TYR A  89      13.514 -12.421   9.506  1.00  3.65
ATOM    662  CD1 TYR A  89      14.351 -12.070  10.567  1.00  3.02
ATOM    663  CE1 TYR A  89      14.291 -12.749  11.779  1.00  4.19
ATOM    664  CD2 TYR A  89      12.631 -13.484   9.687  1.00  3.12
ATOM    665  CE2 TYR A  89      12.567 -14.166  10.896  1.00  2.69
ATOM    666  CZ  TYR A  89      13.386 -13.795  11.935  1.00  2.60
ATOM    667  OH  TYR A  89      13.276 -14.448  13.150  1.00  4.48
ATOM    668  C   TYR A  89      11.436 -12.191   6.856  1.00  6.38
ATOM    669  O   TYR A  89      10.751 -11.521   7.640  1.00  6.58
ATOM    670  N   PRO A  90      10.873 -12.960   5.913  1.00  6.37
ATOM    671  CD  PRO A  90      11.642 -14.007   5.220  1.00  5.17
ATOM    672  CA  PRO A  90       9.446 -13.055   5.582  1.00  6.11
ATOM    673  CB  PRO A  90       9.404 -14.185   4.542  1.00  6.13
ATOM    674  CG  PRO A  90      10.821 -14.238   3.999  1.00  7.30
ATOM    675  C   PRO A  90       8.525 -13.362   6.758  1.00  6.07
ATOM    676  O   PRO A  90       8.938 -13.986   7.734  1.00  7.91
ATOM    677  N   TYR A  91       7.261 -12.957   6.630  1.00  5.44
ATOM    678  CA  TYR A  91       6.257 -13.166   7.672  1.00  5.59
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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 679 | CB | TYR | A | 91 | 5.160 | -12.088 | 7.564 | 1.00 | 2.92 |
| ATOM | 680 | CG | TYR | A | 91 | 4.164 | -12.078 | 8.723 | 1.00 | 2.95 |
| ATOM | 681 | CD1 | TYR | A | 91 | 4.587 | -11.894 | 10.037 | 1.00 | 2.56 |
| ATOM | 682 | CE1 | TYR | A | 91 | 3.685 | -11.911 | 11.093 | 1.00 | 2.00 |
| ATOM | 683 | CD2 | TYR | A | 91 | 2.809 | -12.274 | 8.500 | 1.00 | 3.84 |
| ATOM | 684 | CE2 | TYR | A | 91 | 1.916 | -12.280 | 9.544 | 1.00 | 2.44 |
| ATOM | 685 | CZ | TYR | A | 91 | 2.362 | -12.101 | 10.825 | 1.00 | 2.00 |
| ATOM | 686 | OH | TYR | A | 91 | 1.472 | -12.104 | 11.831 | 1.00 | 2.00 |
| ATOM | 687 | C | TYR | A | 91 | 5.647 | -14.583 | 7.591 | 1.00 | 6.55 |
| ATOM | 688 | O | TYR | A | 91 | 5.337 | -15.061 | 6.514 | 1.00 | 7.52 |
| ATOM | 689 | N | GLU | A | 92 | 5.479 | -15.237 | 8.740 | 1.00 | 9.38 |
| ATOM | 690 | CA | GLU | A | 92 | 4.932 | -16.588 | 8.822 | 1.00 | 9.85 |
| ATOM | 691 | CB | GLU | A | 92 | 5.930 | -17.527 | 9.495 | 1.00 | 12.09 |
| ATOM | 692 | CG | GLU | A | 92 | 7.225 | -17.762 | 8.765 | 1.00 | 16.86 |
| ATOM | 693 | CD | GLU | A | 92 | 8.076 | -18.800 | 9.474 | 1.00 | 18.98 |
| ATOM | 694 | OE1 | GLU | A | 92 | 7.797 | -20.011 | 9.317 | 1.00 | 21.96 |
| ATOM | 695 | OE2 | GLU | A | 92 | 9.011 | -18.408 | 10.202 | 1.00 | 20.31 |
| ATOM | 696 | C | GLU | A | 92 | 3.661 | -16.662 | 9.642 | 1.00 | 9.18 |
| ATOM | 697 | O | GLU | A | 92 | 3.032 | -17.711 | 9.693 | 1.00 | 10.24 |
| ATOM | 698 | N | ALA | A | 93 | 3.334 | -15.587 | 10.347 | 1.00 | 7.87 |
| ATOM | 699 | CA | ALA | A | 93 | 2.147 | -15.537 | 11.201 | 1.00 | 7.08 |
| ATOM | 700 | CB | ALA | A | 93 | 0.854 | -15.664 | 10.375 | 1.00 | 4.50 |
| ATOM | 701 | C | ALA | A | 93 | 2.181 | -16.568 | 12.323 | 1.00 | 6.62 |
| ATOM | 702 | O | ALA | A | 93 | 1.152 | -17.029 | 12.800 | 1.00 | 9.78 |
| ATOM | 703 | N | THR | A | 94 | 3.376 | -16.918 | 12.763 | 1.00 | 8.44 |
| ATOM | 704 | CA | THR | A | 94 | 3.545 | -17.846 | 13.883 | 1.00 | 11.70 |
| ATOM | 705 | CB | THR | A | 94 | 3.692 | -19.320 | 13.417 | 1.00 | 11.68 |
| ATOM | 706 | OG1 | THR | A | 94 | 4.774 | -19.414 | 12.479 | 1.00 | 12.05 |
| ATOM | 707 | CG2 | THR | A | 94 | 2.416 | -19.801 | 12.752 | 1.00 | 13.27 |
| ATOM | 708 | C | THR | A | 94 | 4.825 | -17.430 | 14.620 | 1.00 | 12.43 |
| ATOM | 709 | O | THR | A | 94 | 5.718 | -16.810 | 14.024 | 1.00 | 13.81 |
| ATOM | 710 | N | GLN | A | 95 | 4.888 | -17.705 | 15.915 | 1.00 | 13.02 |
| ATOM | 711 | CA | GLN | A | 95 | 6.066 | -17.361 | 16.690 | 1.00 | 15.16 |
| ATOM | 712 | CB | GLN | A | 95 | 5.711 | -17.195 | 18.173 | 1.00 | 16.05 |
| ATOM | 713 | CG | GLN | A | 95 | 6.850 | -16.641 | 19.033 | 1.00 | 17.89 |
| ATOM | 714 | CD | GLN | A | 95 | 6.479 | -16.486 | 20.499 | 1.00 | 19.00 |
| ATOM | 715 | OE1 | GLN | A | 95 | 5.300 | -16.459 | 20.852 | 1.00 | 21.94 |

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ATOM    716  NE2 GLN A  95       7.480 -16.337  21.350  1.00 19.03
ATOM    717  C   GLN A  95       7.076 -18.489  16.487  1.00 16.17
ATOM    718  O   GLN A  95       6.751 -19.665  16.653  1.00 18.04
ATOM    719  N   GLU A  96       8.281 -18.131  16.072  1.00 14.18
ATOM    720  CA  GLU A  96       9.330 -19.105  15.826  1.00 13.91
ATOM    721  CB  GLU A  96       9.640 -19.144  14.325  1.00 15.91
ATOM    722  CG  GLU A  96       8.500 -19.654  13.423  1.00 18.09
ATOM    723  CD  GLU A  96       8.068 -21.079  13.750  1.00 18.52
ATOM    724  OE1 GLU A  96       8.940 -21.958  13.943  1.00 19.16
ATOM    725  OE2 GLU A  96       6.842 -21.309  13.828  1.00 20.01
ATOM    726  C   GLU A  96      10.579 -18.700  16.603  1.00 12.33
ATOM    727  O   GLU A  96      10.538 -17.747  17.363  1.00 12.46
ATOM    728  N   SER A  97      11.671 -19.438  16.439  1.00 10.38
ATOM    729  CA  SER A  97      12.914 -19.102  17.119  1.00  9.59
ATOM    730  CB  SER A  97      13.895 -20.286  17.092  1.00 10.52
ATOM    731  OG  SER A  97      14.427 -20.483  15.788  1.00 12.03
ATOM    732  C   SER A  97      13.522 -17.912  16.362  1.00  8.39
ATOM    733  O   SER A  97      13.402 -17.817  15.146  1.00  8.25
ATOM    734  N   CYS A  98      14.209 -17.037  17.072  1.00  7.78
ATOM    735  CA  CYS A  98      14.806 -15.860  16.458  1.00  7.77
ATOM    736  C   CYS A  98      15.866 -16.156  15.393  1.00  8.99
ATOM    737  O   CYS A  98      16.832 -16.876  15.661  1.00  7.60
ATOM    738  CB  CYS A  98      15.391 -14.959  17.562  1.00  8.37
ATOM    739  SG  CYS A  98      16.104 -13.391  16.965  1.00  7.51
ATOM    740  N   LYS A  99      15.692 -15.582  14.200  1.00  7.98
ATOM    741  CA  LYS A  99      16.632 -15.766  13.081  1.00  9.08
ATOM    742  CB  LYS A  99      15.932 -16.447  11.887  1.00  9.56
ATOM    743  CG  LYS A  99      15.268 -17.781  12.214  1.00 11.70
ATOM    744  CD  LYS A  99      14.297 -18.219  11.120  1.00 11.75
ATOM    745  CE  LYS A  99      13.536 -19.459  11.539  1.00 12.41
ATOM    746  NZ  LYS A  99      12.876 -19.306  12.863  1.00  9.94
ATOM    747  C   LYS A  99      17.243 -14.436  12.603  1.00  8.47
ATOM    748  O   LYS A  99      17.507 -14.246  11.409  1.00  8.50
ATOM    749  N   TYR A 100      17.435 -13.503  13.525  1.00  8.01
ATOM    750  CA  TYR A 100      18.007 -12.213  13.180  1.00  8.06
ATOM    751  CB  TYR A 100      17.989 -11.260  14.384  1.00  6.33
ATOM    752  CG  TYR A 100      18.754  -9.974  14.101  1.00  5.91
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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 753 | CD1 | TYR | A | 100 | 18.308 | -9.061 | 13.130 | 1.00 | 6.84 |
| ATOM | 754 | CE1 | TYR | A | 100 | 19.042 | -7.897 | 12.835 | 1.00 | 7.37 |
| ATOM | 755 | CD2 | TYR | A | 100 | 19.938 | -9.697 | 14.762 | 1.00 | 4.55 |
| ATOM | 756 | CE2 | TYR | A | 100 | 20.673 | -8.547 | 14.479 | 1.00 | 6.62 |
| ATOM | 757 | CZ | TYR | A | 100 | 20.226 | -7.652 | 13.527 | 1.00 | 6.16 |
| ATOM | 758 | OH | TYR | A | 100 | 20.961 | -6.515 | 13.299 | 1.00 | 6.06 |
| ATOM | 759 | C | TYR | A | 100 | 19.444 | -12.368 | 12.700 | 1.00 | 8.31 |
| ATOM | 760 | O | TYR | A | 100 | 20.244 | -13.051 | 13.340 | 1.00 | 10.14 |
| ATOM | 761 | N | ASN | A | 101 | 19.766 | -11.702 | 11.599 | 1.00 | 9.40 |
| ATOM | 762 | CA | ASN | A | 101 | 21.107 | -11.726 | 11.034 | 1.00 | 11.49 |
| ATOM | 763 | CB | ASN | A | 101 | 21.107 | -12.508 | 9.705 | 1.00 | 12.69 |
| ATOM | 764 | CG | ASN | A | 101 | 22.523 | -12.795 | 9.159 | 1.00 | 12.49 |
| ATOM | 765 | OD1 | ASN | A | 101 | 22.691 | -13.618 | 8.270 | 1.00 | 14.39 |
| ATOM | 766 | ND2 | ASN | A | 101 | 23.523 | -12.111 | 9.676 | 1.00 | 12.32 |
| ATOM | 767 | C | ASN | A | 101 | 21.502 | -10.271 | 10.791 | 1.00 | 11.92 |
| ATOM | 768 | O | ASN | A | 101 | 20.835 | -9.571 | 10.038 | 1.00 | 12.70 |
| ATOM | 769 | N | PRO | A | 102 | 22.597 | -9.800 | 11.427 | 1.00 | 13.21 |
| ATOM | 770 | CD | PRO | A | 102 | 23.429 | -10.561 | 12.382 | 1.00 | 13.68 |
| ATOM | 771 | CA | PRO | A | 102 | 23.093 | -8.422 | 11.282 | 1.00 | 14.35 |
| ATOM | 772 | CB | PRO | A | 102 | 24.413 | -8.447 | 12.068 | 1.00 | 14.93 |
| ATOM | 773 | CG | PRO | A | 102 | 24.190 | -9.480 | 13.113 | 1.00 | 14.61 |
| ATOM | 774 | C | PRO | A | 102 | 23.352 | -8.022 | 9.823 | 1.00 | 15.86 |
| ATOM | 775 | O | PRO | A | 102 | 23.165 | -6.874 | 9.435 | 1.00 | 14.62 |
| ATOM | 776 | N | LYS | A | 103 | 23.790 | -8.987 | 9.025 | 1.00 | 16.95 |
| ATOM | 777 | CA | LYS | A | 103 | 24.107 | -8.764 | 7.617 | 1.00 | 18.84 |
| ATOM | 778 | CB | LYS | A | 103 | 24.622 | -10.069 | 7.006 | 1.00 | 19.74 |
| ATOM | 779 | CG | LYS | A | 103 | 24.913 | -10.027 | 5.520 | 1.00 | 20.69 |
| ATOM | 780 | CD | LYS | A | 103 | 25.891 | -11.136 | 5.170 | 1.00 | 23.17 |
| ATOM | 781 | CE | LYS | A | 103 | 25.733 | -11.617 | 3.747 | 1.00 | 24.09 |
| ATOM | 782 | NZ | LYS | A | 103 | 24.445 | -12.343 | 3.588 | 1.00 | 25.55 |
| ATOM | 783 | C | LYS | A | 103 | 22.961 | -8.206 | 6.777 | 1.00 | 17.53 |
| ATOM | 784 | O | LYS | A | 103 | 23.188 | -7.536 | 5.771 | 1.00 | 18.99 |
| ATOM | 785 | N | TYR | A | 104 | 21.735 | -8.465 | 7.209 | 1.00 | 16.09 |
| ATOM | 786 | CA | TYR | A | 104 | 20.547 | -8.015 | 6.497 | 1.00 | 13.93 |
| ATOM | 787 | CB | TYR | A | 104 | 19.631 | -9.226 | 6.265 | 1.00 | 17.19 |
| ATOM | 788 | CG | TYR | A | 104 | 20.233 | -10.289 | 5.368 | 1.00 | 18.52 |
| ATOM | 789 | CD1 | TYR | A | 104 | 20.715 | -11.497 | 5.891 | 1.00 | 20.01 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| ATOM | 790 | CE1 | TYR | A | 104 | 21.272 | -12.488 | 5.041 | 1.00 20.46 |
| ATOM | 791 | CD2 | TYR | A | 104 | 20.320 | -10.085 | 3.992 | 1.00 18.97 |
| ATOM | 792 | CE2 | TYR | A | 104 | 20.867 | -11.048 | 3.149 | 1.00 21.11 |
| ATOM | 793 | CZ | TYR | A | 104 | 21.341 | -12.247 | 3.670 | 1.00 21.22 |
| ATOM | 794 | OH | TYR | A | 104 | 21.858 | -13.186 | 2.797 | 1.00 22.83 |
| ATOM | 795 | C | TYR | A | 104 | 19.774 | -6.894 | 7.215 | 1.00 12.09 |
| ATOM | 796 | O | TYR | A | 104 | 18.623 | -6.611 | 6.870 | 1.00 11.05 |
| ATOM | 797 | N | SER | A | 105 | 20.393 | -6.286 | 8.226 | 1.00 10.05 |
| ATOM | 798 | CA | SER | A | 105 | 19.774 | -5.212 | 8.989 | 1.00 10.12 |
| ATOM | 799 | CB | SER | A | 105 | 20.592 | -4.935 | 10.246 | 1.00 10.22 |
| ATOM | 800 | OG | SER | A | 105 | 19.972 | -3.966 | 11.069 | 1.00 13.32 |
| ATOM | 801 | C | SER | A | 105 | 19.660 | -3.957 | 8.115 | 1.00 10.60 |
| ATOM | 802 | O | SER | A | 105 | 20.635 | -3.513 | 7.520 | 1.00 10.42 |
| ATOM | 803 | N | VAL | A | 106 | 18.459 | -3.392 | 8.026 | 1.00 11.25 |
| ATOM | 804 | CA | VAL | A | 106 | 18.229 | -2.222 | 7.186 | 1.00 8.73 |
| ATOM | 805 | CB | VAL | A | 106 | 17.268 | -2.551 | 6.038 | 1.00 9.27 |
| ATOM | 806 | CG1 | VAL | A | 106 | 17.970 | -3.393 | 4.967 | 1.00 9.09 |
| ATOM | 807 | CG2 | VAL | A | 106 | 16.039 | -3.257 | 6.587 | 1.00 7.79 |
| ATOM | 808 | C | VAL | A | 106 | 17.655 | -1.036 | 7.945 | 1.00 8.47 |
| ATOM | 809 | O | VAL | A | 106 | 17.406 | 0.013 | 7.374 | 1.00 7.49 |
| ATOM | 810 | N | ALA | A | 107 | 17.472 | -1.187 | 9.243 | 1.00 9.35 |
| ATOM | 811 | CA | ALA | A | 107 | 16.909 | -0.113 | 10.024 | 1.00 7.88 |
| ATOM | 812 | CB | ALA | A | 107 | 15.390 | -0.239 | 10.045 | 1.00 9.12 |
| ATOM | 813 | C | ALA | A | 107 | 17.472 | -0.219 | 11.416 | 1.00 8.09 |
| ATOM | 814 | O | ALA | A | 107 | 18.091 | -1.228 | 11.748 | 1.00 7.87 |
| ATOM | 815 | N | ASN | A | 108 | 17.326 | 0.849 | 12.192 | 1.00 6.12 |
| ATOM | 816 | CA | ASN | A | 108 | 17.791 | 0.887 | 13.569 | 1.00 8.13 |
| ATOM | 817 | CB | ASN | A | 108 | 19.330 | 1.046 | 13.632 | 1.00 9.44 |
| ATOM | 818 | CG | ASN | A | 108 | 19.928 | 0.521 | 14.941 | 1.00 11.94 |
| ATOM | 819 | OD1 | ASN | A | 108 | 19.209 | 0.130 | 15.878 | 1.00 10.93 |
| ATOM | 820 | ND2 | ASN | A | 108 | 21.254 | 0.480 | 15.001 | 1.00 14.47 |
| ATOM | 821 | C | ASN | A | 108 | 17.109 | 2.075 | 14.241 | 1.00 7.01 |
| ATOM | 822 | O | ASN | A | 108 | 16.512 | 2.912 | 13.569 | 1.00 7.52 |
| ATOM | 823 | N | ASP | A | 109 | 17.092 | 2.085 | 15.564 | 1.00 6.13 |
| ATOM | 824 | CA | ASP | A | 109 | 16.510 | 3.200 | 16.274 | 1.00 5.45 |
| ATOM | 825 | CB | ASP | A | 109 | 14.966 | 3.170 | 16.292 | 1.00 3.96 |
| ATOM | 826 | CG | ASP | A | 109 | 14.376 | 2.083 | 17.150 | 1.00 2.00 |

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|---|---|---|---|---|---|---|---|---|---|---|
| | ATOM | 827 | OD1 | ASP | A | 109 | 14.779 | 1.877 | 18.307 | 1.00 | 2.00 |
| | ATOM | 828 | OD2 | ASP | A | 109 | 13.421 | 1.471 | 16.669 | 1.00 | 6.11 |
| | ATOM | 829 | C | ASP | A | 109 | 17.192 | 3.358 | 17.627 | 1.00 | 6.97 |
| | ATOM | 830 | O | ASP | A | 109 | 17.946 | 2.476 | 18.041 | 1.00 | 5.45 |
| 5 | ATOM | 831 | N | THR | A | 110 | 17.063 | 4.552 | 18.209 | 1.00 | 7.11 |
| | ATOM | 832 | CA | THR | A | 110 | 17.696 | 4.899 | 19.473 | 1.00 | 6.66 |
| | ATOM | 833 | CB | THR | A | 110 | 18.530 | 6.197 | 19.288 | 1.00 | 8.79 |
| | ATOM | 834 | OG1 | THR | A | 110 | 17.690 | 7.243 | 18.765 | 1.00 | 10.79 |
| | ATOM | 835 | CG2 | THR | A | 110 | 19.686 | 5.948 | 18.294 | 1.00 | 7.34 |
| 10 | ATOM | 836 | C | THR | A | 110 | 16.718 | 5.066 | 20.628 | 1.00 | 4.62 |
| | ATOM | 837 | O | THR | A | 110 | 17.040 | 5.672 | 21.651 | 1.00 | 5.93 |
| | ATOM | 838 | N | GLY | A | 111 | 15.534 | 4.493 | 20.468 | 1.00 | 3.74 |
| | ATOM | 839 | CA | GLY | A | 111 | 14.520 | 4.596 | 21.488 | 1.00 | 2.67 |
| | ATOM | 840 | C | GLY | A | 111 | 13.192 | 4.986 | 20.884 | 1.00 | 2.00 |
| 15 | ATOM | 841 | O | GLY | A | 111 | 12.893 | 4.724 | 19.735 | 1.00 | 2.70 |
| | ATOM | 842 | N | PHE | A | 112 | 12.362 | 5.626 | 21.671 | 1.00 | 4.56 |
| | ATOM | 843 | CA | PHE | A | 112 | 11.062 | 6.011 | 21.178 | 1.00 | 5.16 |
| | ATOM | 844 | CB | PHE | A | 112 | 10.088 | 4.841 | 21.343 | 1.00 | 4.13 |
| | ATOM | 845 | CG | PHE | A | 112 | 10.111 | 4.234 | 22.711 | 1.00 | 4.90 |
| 20 | ATOM | 846 | CD1 | PHE | A | 112 | 9.210 | 4.650 | 23.688 | 1.00 | 3.88 |
| | ATOM | 847 | CD2 | PHE | A | 112 | 11.054 | 3.254 | 23.031 | 1.00 | 5.14 |
| | ATOM | 848 | CE1 | PHE | A | 112 | 9.240 | 4.116 | 24.949 | 1.00 | 4.07 |
| | ATOM | 849 | CE2 | PHE | A | 112 | 11.099 | 2.705 | 24.292 | 1.00 | 4.00 |
| | ATOM | 850 | CZ | PHE | A | 112 | 10.194 | 3.134 | 25.262 | 1.00 | 6.43 |
| 25 | ATOM | 851 | C | PHE | A | 112 | 10.570 | 7.228 | 21.937 | 1.00 | 5.13 |
| | ATOM | 852 | O | PHE | A | 112 | 11.104 | 7.591 | 22.994 | 1.00 | 4.21 |
| | ATOM | 853 | N | VAL | A | 113 | 9.544 | 7.849 | 21.379 | 1.00 | 6.86 |
| | ATOM | 854 | CA | VAL | A | 113 | 8.939 | 9.027 | 21.962 | 1.00 | 5.63 |
| | ATOM | 855 | CB | VAL | A | 113 | 9.097 | 10.241 | 21.002 | 1.00 | 5.64 |
| 30 | ATOM | 856 | CG1 | VAL | A | 113 | 8.347 | 11.460 | 21.525 | 1.00 | 5.46 |
| | ATOM | 857 | CG2 | VAL | A | 113 | 10.563 | 10.556 | 20.801 | 1.00 | 2.00 |
| | ATOM | 858 | C | VAL | A | 113 | 7.469 | 8.737 | 22.181 | 1.00 | 4.33 |
| | ATOM | 859 | O | VAL | A | 113 | 6.783 | 8.356 | 21.253 | 1.00 | 6.32 |
| | ATOM | 860 | N | ASP | A | 114 | 7.022 | 8.804 | 23.425 | 1.00 | 2.00 |
| 35 | ATOM | 861 | CA | ASP | A | 114 | 5.618 | 8.602 | 23.750 | 1.00 | 2.83 |
| | ATOM | 862 | CB | ASP | A | 114 | 5.458 | 8.046 | 25.178 | 1.00 | 3.20 |
| | ATOM | 863 | CG | ASP | A | 114 | 5.817 | 6.549 | 25.286 | 1.00 | 3.67 |

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|---|---|---|---|---|---|---|---|---|---|---|
| | ATOM | 864 | OD1 | ASP | A | 114 | 5.806 | 5.838 | 24.262 | 1.00 | 3.11 |
| | ATOM | 865 | OD2 | ASP | A | 114 | 6.080 | 6.080 | 26.406 | 1.00 | 6.65 |
| | ATOM | 866 | C | ASP | A | 114 | 4.918 | 9.976 | 23.637 | 1.00 | 4.44 |
| | ATOM | 867 | O | ASP | A | 114 | 5.354 | 10.961 | 24.232 | 1.00 | 2.19 |
| 5 | ATOM | 868 | N | ILE | A | 115 | 3.847 | 10.039 | 22.853 | 1.00 | 6.03 |
| | ATOM | 869 | CA | ILE | A | 115 | 3.101 | 11.285 | 22.652 | 1.00 | 5.07 |
| | ATOM | 870 | CB | ILE | A | 115 | 2.382 | 11.224 | 21.309 | 1.00 | 4.23 |
| | ATOM | 871 | CG2 | ILE | A | 115 | 1.486 | 12.448 | 21.094 | 1.00 | 5.61 |
| | ATOM | 872 | CG1 | ILE | A | 115 | 3.428 | 11.123 | 20.205 | 1.00 | 5.06 |
| 10 | ATOM | 873 | CD1 | ILE | A | 115 | 2.867 | 10.800 | 18.908 | 1.00 | 7.50 |
| | ATOM | 874 | C | ILE | A | 115 | 2.121 | 11.503 | 23.814 | 1.00 | 6.10 |
| | ATOM | 875 | O | ILE | A | 115 | 1.528 | 10.549 | 24.305 | 1.00 | 5.98 |
| | ATOM | 876 | N | PRO | A | 116 | 2.059 | 12.730 | 24.378 | 1.00 | 6.30 |
| | ATOM | 877 | CD | PRO | A | 116 | 2.848 | 13.952 | 24.111 | 1.00 | 5.18 |
| 15 | ATOM | 878 | CA | PRO | A | 116 | 1.115 | 12.930 | 25.489 | 1.00 | 5.18 |
| | ATOM | 879 | CB | PRO | A | 116 | 1.195 | 14.443 | 25.739 | 1.00 | 6.41 |
| | ATOM | 880 | CG | PRO | A | 116 | 2.629 | 14.761 | 25.357 | 1.00 | 5.36 |
| | ATOM | 881 | C | PRO | A | 116 | -0.295 | 12.466 | 25.088 | 1.00 | 4.51 |
| | ATOM | 882 | O | PRO | A | 116 | -0.625 | 12.406 | 23.903 | 1.00 | 5.58 |
| 20 | ATOM | 883 | N | LYS | A | 117 | -1.118 | 12.143 | 26.077 | 1.00 | 5.49 |
| | ATOM | 884 | CA | LYS | A | 117 | -2.487 | 11.650 | 25.856 | 1.00 | 7.56 |
| | ATOM | 885 | CB | LYS | A | 117 | -2.994 | 10.896 | 27.117 | 1.00 | 8.77 |
| | ATOM | 886 | CG | LYS | A | 117 | -4.399 | 10.264 | 26.949 | 1.00 | 13.73 |
| | ATOM | 887 | CD | LYS | A | 117 | -4.762 | 9.319 | 28.085 | 1.00 | 18.24 |
| 25 | ATOM | 888 | CE | LYS | A | 117 | -6.085 | 8.595 | 27.842 | 1.00 | 20.02 |
| | ATOM | 889 | NZ | LYS | A | 117 | -6.223 | 7.470 | 28.831 | 1.00 | 23.28 |
| | ATOM | 890 | C | LYS | A | 117 | -3.464 | 12.769 | 25.456 | 1.00 | 4.15 |
| | ATOM | 891 | O | LYS | A | 117 | -4.478 | 12.986 | 26.105 | 1.00 | 3.78 |
| | ATOM | 892 | N | GLN | A | 118 | -3.192 | 13.408 | 24.330 | 1.00 | 4.63 |
| 30 | ATOM | 893 | CA | GLN | A | 118 | -4.006 | 14.523 | 23.854 | 1.00 | 2.00 |
| | ATOM | 894 | CB | GLN | A | 118 | -3.320 | 15.848 | 24.246 | 1.00 | 2.19 |
| | ATOM | 895 | CG | GLN | A | 118 | -3.156 | 16.116 | 25.746 | 1.00 | 2.00 |
| | ATOM | 896 | CD | GLN | A | 118 | -4.465 | 16.517 | 26.381 | 1.00 | 2.00 |
| | ATOM | 897 | OE1 | GLN | A | 118 | -5.451 | 16.770 | 25.687 | 1.00 | 2.00 |
| 35 | ATOM | 898 | NE2 | GLN | A | 118 | -4.487 | 16.583 | 27.701 | 1.00 | 3.75 |
| | ATOM | 899 | C | GLN | A | 118 | -4.097 | 14.443 | 22.328 | 1.00 | 2.00 |
| | ATOM | 900 | O | GLN | A | 118 | -3.067 | 14.348 | 21.662 | 1.00 | 2.66 |

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 901 | N | GLN A 119 | -5.309 | 14.512 | 21.771 | 1.00 | 2.34 |
| ATOM | 902 | CA | GLN A 119 | -5.472 | 14.465 | 20.313 | 1.00 | 2.40 |
| ATOM | 903 | CB | GLN A 119 | -6.943 | 14.372 | 19.926 | 1.00 | 2.69 |
| ATOM | 904 | CG | GLN A 119 | -7.502 | 12.969 | 20.122 | 1.00 | 3.44 |
| ATOM | 905 | CD | GLN A 119 | -8.863 | 12.793 | 19.527 | 1.00 | 2.00 |
| ATOM | 906 | OE1 | GLN A 119 | -9.013 | 12.378 | 18.386 | 1.00 | 2.00 |
| ATOM | 907 | NE2 | GLN A 119 | -9.869 | 13.108 | 20.298 | 1.00 | 2.00 |
| ATOM | 908 | C | GLN A 119 | -4.782 | 15.649 | 19.623 | 1.00 | 3.36 |
| ATOM | 909 | O | GLN A 119 | -4.364 | 15.539 | 18.462 | 1.00 | 5.13 |
| ATOM | 910 | N | LYS A 120 | -4.609 | 16.756 | 20.347 | 1.00 | 2.61 |
| ATOM | 911 | CA | LYS A 120 | -3.911 | 17.923 | 19.785 | 1.00 | 3.92 |
| ATOM | 912 | CB | LYS A 120 | -4.161 | 19.204 | 20.616 | 1.00 | 2.00 |
| ATOM | 913 | CG | LYS A 120 | -5.561 | 19.762 | 20.445 | 1.00 | 2.42 |
| ATOM | 914 | CD | LYS A 120 | -5.637 | 21.206 | 20.846 | 1.00 | 2.46 |
| ATOM | 915 | CE | LYS A 120 | -6.904 | 21.849 | 20.283 | 1.00 | 3.62 |
| ATOM | 916 | NZ | LYS A 120 | -8.149 | 21.447 | 21.007 | 1.00 | 2.56 |
| ATOM | 917 | C | LYS A 120 | -2.413 | 17.618 | 19.673 | 1.00 | 2.00 |
| ATOM | 918 | O | LYS A 120 | -1.776 | 17.936 | 18.663 | 1.00 | 2.00 |
| ATOM | 919 | N | ALA A 121 | -1.872 | 16.955 | 20.688 | 1.00 | 2.00 |
| ATOM | 920 | CA | ALA A 121 | -0.460 | 16.584 | 20.672 | 1.00 | 4.18 |
| ATOM | 921 | CB | ALA A 121 | -0.019 | 16.040 | 22.027 | 1.00 | 2.84 |
| ATOM | 922 | C | ALA A 121 | -0.266 | 15.545 | 19.567 | 1.00 | 4.14 |
| ATOM | 923 | O | ALA A 121 | 0.717 | 15.597 | 18.834 | 1.00 | 5.32 |
| ATOM | 924 | N | LEU A 122 | -1.221 | 14.631 | 19.407 | 1.00 | 3.62 |
| ATOM | 925 | CA | LEU A 122 | -1.105 | 13.634 | 18.350 | 1.00 | 3.75 |
| ATOM | 926 | CB | LEU A 122 | -2.198 | 12.558 | 18.463 | 1.00 | 3.20 |
| ATOM | 927 | CG | LEU A 122 | -2.192 | 11.487 | 17.358 | 1.00 | 2.55 |
| ATOM | 928 | CD1 | LEU A 122 | -0.839 | 10.769 | 17.325 | 1.00 | 2.00 |
| ATOM | 929 | CD2 | LEU A 122 | -3.350 | 10.508 | 17.585 | 1.00 | 2.00 |
| ATOM | 930 | C | LEU A 122 | -1.161 | 14.306 | 16.981 | 1.00 | 3.37 |
| ATOM | 931 | O | LEU A 122 | -0.415 | 13.944 | 16.078 | 1.00 | 5.98 |
| ATOM | 932 | N | MET A 123 | -2.008 | 15.317 | 16.824 | 1.00 | 4.16 |
| ATOM | 933 | CA | MET A 123 | -2.109 | 15.986 | 15.524 | 1.00 | 4.50 |
| ATOM | 934 | CB | MET A 123 | -3.300 | 16.967 | 15.492 | 1.00 | 2.00 |
| ATOM | 935 | CG | MET A 123 | -3.328 | 17.826 | 14.240 | 1.00 | 6.09 |
| ATOM | 936 | SD | MET A 123 | -4.804 | 18.832 | 14.011 | 1.00 | 7.73 |
| ATOM | 937 | CE | MET A 123 | -4.871 | 19.690 | 15.533 | 1.00 | 11.61 |

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 938 | C | MET | A | 123 | -0.793 | 16.678 | 15.145 | 1.00 | 4.46 |
| ATOM | 939 | O | MET | A | 123 | -0.304 | 16.543 | 14.024 | 1.00 | 4.89 |
| ATOM | 940 | N | LYS | A | 124 | -0.195 | 17.380 | 16.101 | 1.00 | 6.80 |
| ATOM | 941 | CA | LYS | A | 124 | 1.069 | 18.061 | 15.843 | 1.00 | 9.63 |
| ATOM | 942 | CB | LYS | A | 124 | 1.492 | 18.927 | 17.040 | 1.00 | 11.48 |
| ATOM | 943 | CG | LYS | A | 124 | 2.818 | 19.642 | 16.823 | 1.00 | 13.66 |
| ATOM | 944 | CD | LYS | A | 124 | 3.303 | 20.297 | 18.094 | 1.00 | 19.45 |
| ATOM | 945 | CE | LYS | A | 124 | 4.791 | 20.710 | 17.993 | 1.00 | 23.17 |
| ATOM | 946 | NZ | LYS | A | 124 | 5.758 | 19.550 | 17.946 | 1.00 | 25.70 |
| ATOM | 947 | C | LYS | A | 124 | 2.167 | 17.035 | 15.520 | 1.00 | 9.28 |
| ATOM | 948 | O | LYS | A | 124 | 2.959 | 17.241 | 14.597 | 1.00 | 9.70 |
| ATOM | 949 | N | ALA | A | 125 | 2.213 | 15.931 | 16.267 | 1.00 | 7.34 |
| ATOM | 950 | CA | ALA | A | 125 | 3.224 | 14.914 | 16.011 | 1.00 | 5.80 |
| ATOM | 951 | CB | ALA | A | 125 | 3.195 | 13.821 | 17.077 | 1.00 | 6.66 |
| ATOM | 952 | C | ALA | A | 125 | 3.048 | 14.323 | 14.616 | 1.00 | 4.87 |
| ATOM | 953 | O | ALA | A | 125 | 4.017 | 14.223 | 13.883 | 1.00 | 5.44 |
| ATOM | 954 | N | VAL | A | 126 | 1.823 | 13.988 | 14.220 | 1.00 | 5.20 |
| ATOM | 955 | CA | VAL | A | 126 | 1.600 | 13.433 | 12.884 | 1.00 | 3.43 |
| ATOM | 956 | CB | VAL | A | 126 | 0.140 | 12.948 | 12.668 | 1.00 | 3.05 |
| ATOM | 957 | CG1 | VAL | A | 126 | -0.046 | 12.439 | 11.221 | 1.00 | 2.65 |
| ATOM | 958 | CG2 | VAL | A | 126 | -0.196 | 11.830 | 13.655 | 1.00 | 3.06 |
| ATOM | 959 | C | VAL | A | 126 | 1.939 | 14.472 | 11.820 | 1.00 | 6.95 |
| ATOM | 960 | O | VAL | A | 126 | 2.379 | 14.118 | 10.734 | 1.00 | 7.09 |
| ATOM | 961 | N | ALA | A | 127 | 1.703 | 15.751 | 12.119 | 1.00 | 6.76 |
| ATOM | 962 | CA | ALA | A | 127 | 2.005 | 16.822 | 11.176 | 1.00 | 7.26 |
| ATOM | 963 | CB | ALA | A | 127 | 1.314 | 18.118 | 11.603 | 1.00 | 7.59 |
| ATOM | 964 | C | ALA | A | 127 | 3.507 | 17.066 | 10.990 | 1.00 | 5.89 |
| ATOM | 965 | O | ALA | A | 127 | 3.935 | 17.443 | 9.912 | 1.00 | 6.40 |
| ATOM | 966 | N | THR | A | 128 | 4.308 | 16.814 | 12.019 | 1.00 | 7.92 |
| ATOM | 967 | CA | THR | A | 128 | 5.765 | 17.052 | 11.954 | 1.00 | 10.10 |
| ATOM | 968 | CB | THR | A | 128 | 6.262 | 17.948 | 13.163 | 1.00 | 11.96 |
| ATOM | 969 | OG1 | THR | A | 128 | 5.849 | 17.385 | 14.423 | 1.00 | 13.80 |
| ATOM | 970 | CG2 | THR | A | 128 | 5.720 | 19.374 | 13.052 | 1.00 | 13.51 |
| ATOM | 971 | C | THR | A | 128 | 6.734 | 15.848 | 11.841 | 1.00 | 9.92 |
| ATOM | 972 | O | THR | A | 128 | 7.799 | 15.954 | 11.224 | 1.00 | 11.85 |
| ATOM | 973 | N | VAL | A | 129 | 6.374 | 14.715 | 12.431 | 1.00 | 6.76 |
| ATOM | 974 | CA | VAL | A | 129 | 7.251 | 13.538 | 12.444 | 1.00 | 5.98 |

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 975 | CB | VAL | A | 129 | 7.077 | 12.775 | 13.803 | 1.00 | 6.66 |
| ATOM | 976 | CG1 | VAL | A | 129 | 7.995 | 11.582 | 13.878 | 1.00 | 7.83 |
| ATOM | 977 | CG2 | VAL | A | 129 | 7.321 | 13.729 | 14.978 | 1.00 | 3.94 |
| ATOM | 978 | C | VAL | A | 129 | 7.057 | 12.579 | 11.274 | 1.00 | 5.16 |
| ATOM | 979 | O | VAL | A | 129 | 8.003 | 12.267 | 10.536 | 1.00 | 3.57 |
| ATOM | 980 | N | GLY | A | 130 | 5.815 | 12.128 | 11.113 | 1.00 | 4.51 |
| ATOM | 981 | CA | GLY | A | 130 | 5.464 | 11.177 | 10.071 | 1.00 | 4.27 |
| ATOM | 982 | C | GLY | A | 130 | 4.451 | 10.202 | 10.649 | 1.00 | 2.84 |
| ATOM | 983 | O | GLY | A | 130 | 3.725 | 10.579 | 11.564 | 1.00 | 2.22 |
| ATOM | 984 | N | PRO | A | 131 | 4.333 | 8.965 | 10.120 | 1.00 | 3.68 |
| ATOM | 985 | CD | PRO | A | 131 | 4.854 | 8.503 | 8.828 | 1.00 | 2.00 |
| ATOM | 986 | CA | PRO | A | 131 | 3.371 | 7.989 | 10.657 | 1.00 | 2.96 |
| ATOM | 987 | CB | PRO | A | 131 | 3.589 | 6.769 | 9.766 | 1.00 | 2.00 |
| ATOM | 988 | CG | PRO | A | 131 | 3.863 | 7.388 | 8.476 | 1.00 | 2.00 |
| ATOM | 989 | C | PRO | A | 131 | 3.644 | 7.694 | 12.121 | 1.00 | 3.70 |
| ATOM | 990 | O | PRO | A | 131 | 4.797 | 7.573 | 12.539 | 1.00 | 4.24 |
| ATOM | 991 | N | ILE | A | 132 | 2.573 | 7.620 | 12.905 | 1.00 | 3.90 |
| ATOM | 992 | CA | ILE | A | 132 | 2.681 | 7.384 | 14.337 | 1.00 | 4.11 |
| ATOM | 993 | CB | ILE | A | 132 | 2.049 | 8.564 | 15.136 | 1.00 | 2.00 |
| ATOM | 994 | CG2 | ILE | A | 132 | 2.125 | 8.309 | 16.617 | 1.00 | 2.00 |
| ATOM | 995 | CG1 | ILE | A | 132 | 2.744 | 9.891 | 14.786 | 1.00 | 2.78 |
| ATOM | 996 | CD1 | ILE | A | 132 | 4.212 | 9.972 | 15.139 | 1.00 | 2.14 |
| ATOM | 997 | C | ILE | A | 132 | 1.988 | 6.094 | 14.758 | 1.00 | 3.87 |
| ATOM | 998 | O | ILE | A | 132 | 0.860 | 5.819 | 14.329 | 1.00 | 2.00 |
| ATOM | 999 | N | SER | A | 133 | 2.652 | 5.326 | 15.619 | 1.00 | 4.96 |
| ATOM | 1000 | CA | SER | A | 133 | 2.075 | 4.069 | 16.127 | 1.00 | 4.29 |
| ATOM | 1001 | CB | SER | A | 133 | 3.154 | 3.144 | 16.740 | 1.00 | 2.00 |
| ATOM | 1002 | OG | SER | A | 133 | 4.018 | 2.578 | 15.753 | 1.00 | 2.10 |
| ATOM | 1003 | C | SER | A | 133 | 1.056 | 4.431 | 17.204 | 1.00 | 4.66 |
| ATOM | 1004 | O | SER | A | 133 | 1.341 | 5.282 | 18.050 | 1.00 | 2.00 |
| ATOM | 1005 | N | VAL | A | 134 | -0.140 | 3.830 | 17.144 | 1.00 | 4.16 |
| ATOM | 1006 | CA | VAL | A | 134 | -1.185 | 4.086 | 18.144 | 1.00 | 3.52 |
| ATOM | 1007 | CB | VAL | A | 134 | -2.257 | 5.151 | 17.657 | 1.00 | 2.00 |
| ATOM | 1008 | CG1 | VAL | A | 134 | -1.614 | 6.480 | 17.286 | 1.00 | 2.31 |
| ATOM | 1009 | CG2 | VAL | A | 134 | -3.044 | 4.626 | 16.486 | 1.00 | 2.00 |
| ATOM | 1010 | C | VAL | A | 134 | -1.942 | 2.787 | 18.480 | 1.00 | 2.44 |
| ATOM | 1011 | O | VAL | A | 134 | -1.969 | 1.863 | 17.682 | 1.00 | 2.81 |

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1012 | N | ALA | A | 135 | -2.523 | 2.720 | 19.673 | 1.00 | 5.76 |
| ATOM | 1013 | CA | ALA | A | 135 | -3.318 | 1.572 | 20.100 | 1.00 | 4.17 |
| ATOM | 1014 | CB | ALA | A | 135 | -2.886 | 1.073 | 21.492 | 1.00 | 3.22 |
| ATOM | 1015 | C | ALA | A | 135 | -4.745 | 2.108 | 20.143 | 1.00 | 4.79 |
| ATOM | 1016 | O | ALA | A | 135 | -4.979 | 3.233 | 20.577 | 1.00 | 3.61 |
| ATOM | 1017 | N | ILE | A | 136 | -5.677 | 1.333 | 19.605 | 1.00 | 4.86 |
| ATOM | 1018 | CA | ILE | A | 136 | -7.073 | 1.713 | 19.573 | 1.00 | 5.26 |
| ATOM | 1019 | CB | ILE | A | 136 | -7.580 | 1.995 | 18.112 | 1.00 | 5.16 |
| ATOM | 1020 | CG2 | ILE | A | 136 | -6.956 | 3.271 | 17.532 | 1.00 | 4.00 |
| ATOM | 1021 | CG1 | ILE | A | 136 | -7.283 | 0.792 | 17.187 | 1.00 | 4.19 |
| ATOM | 1022 | CD1 | ILE | A | 136 | -8.125 | 0.762 | 15.964 | 1.00 | 2.00 |
| ATOM | 1023 | C | ILE | A | 136 | -7.877 | 0.539 | 20.100 | 1.00 | 5.77 |
| ATOM | 1024 | O | ILE | A | 136 | -7.373 | -0.590 | 20.236 | 1.00 | 5.42 |
| ATOM | 1025 | N | ASP | A | 137 | -9.126 | 0.823 | 20.422 | 1.00 | 6.93 |
| ATOM | 1026 | CA | ASP | A | 137 | -10.058 | -0.186 | 20.873 | 1.00 | 7.89 |
| ATOM | 1027 | CB | ASP | A | 137 | -11.068 | 0.413 | 21.858 | 1.00 | 7.84 |
| ATOM | 1028 | CG | ASP | A | 137 | -12.253 | -0.518 | 22.135 | 1.00 | 7.68 |
| ATOM | 1029 | OD1 | ASP | A | 137 | -12.222 | -1.699 | 21.730 | 1.00 | 6.28 |
| ATOM | 1030 | OD2 | ASP | A | 137 | -13.223 | -0.069 | 22.772 | 1.00 | 8.41 |
| ATOM | 1031 | C | ASP | A | 137 | -10.768 | -0.642 | 19.601 | 1.00 | 6.71 |
| ATOM | 1032 | O | ASP | A | 137 | -11.595 | 0.075 | 19.061 | 1.00 | 9.07 |
| ATOM | 1033 | N | ALA | A | 138 | -10.378 | -1.811 | 19.100 | 1.00 | 6.39 |
| ATOM | 1034 | CA | ALA | A | 138 | -10.968 | -2.415 | 17.902 | 1.00 | 5.19 |
| ATOM | 1035 | CB | ALA | A | 138 | -9.851 | -2.929 | 17.020 | 1.00 | 4.89 |
| ATOM | 1036 | C | ALA | A | 138 | -11.905 | -3.580 | 18.269 | 1.00 | 4.07 |
| ATOM | 1037 | O | ALA | A | 138 | -12.399 | -4.285 | 17.405 | 1.00 | 5.91 |
| ATOM | 1038 | N | GLY | A | 139 | -12.148 | -3.772 | 19.562 | 1.00 | 5.00 |
| ATOM | 1039 | CA | GLY | A | 139 | -12.969 | -4.881 | 20.006 | 1.00 | 3.58 |
| ATOM | 1040 | C | GLY | A | 139 | -14.465 | -4.785 | 19.849 | 1.00 | 3.51 |
| ATOM | 1041 | O | GLY | A | 139 | -15.181 | -5.031 | 20.808 | 1.00 | 4.90 |
| ATOM | 1042 | N | HIS | A | 140 | -14.949 | -4.409 | 18.672 | 1.00 | 3.36 |
| ATOM | 1043 | CA | HIS | A | 140 | -16.388 | -4.317 | 18.440 | 1.00 | 3.34 |
| ATOM | 1044 | CB | HIS | A | 140 | -16.900 | -2.878 | 18.608 | 1.00 | 2.00 |
| ATOM | 1045 | CG | HIS | A | 140 | -16.680 | -2.323 | 19.982 | 1.00 | 2.00 |
| ATOM | 1046 | CD2 | HIS | A | 140 | -17.465 | -2.330 | 21.081 | 1.00 | 2.00 |
| ATOM | 1047 | ND1 | HIS | A | 140 | -15.472 | -1.791 | 20.378 | 1.00 | 3.34 |
| ATOM | 1048 | CE1 | HIS | A | 140 | -15.515 | -1.511 | 21.670 | 1.00 | 2.59 |

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|---|---|---|---|---|---|---|---|---|---|---|
| | ATOM | 1049 | NE2 | HIS | A | 140 | -16.715 | -1.829 | 22.117 | 1.00 | 2.18 |
| | ATOM | 1050 | C | HIS | A | 140 | -16.636 | -4.809 | 17.043 | 1.00 | 3.99 |
| | ATOM | 1051 | O | HIS | A | 140 | -15.779 | -4.657 | 16.188 | 1.00 | 6.59 |
| | ATOM | 1052 | N | GLU | A | 141 | -17.775 | -5.450 | 16.818 | 1.00 | 6.39 |
| | ATOM | 1053 | CA | GLU | A | 141 | -18.123 | -5.952 | 15.490 | 1.00 | 7.99 |
| | ATOM | 1054 | CB | GLU | A | 141 | -19.462 | -6.687 | 15.539 | 1.00 | 11.94 |
| | ATOM | 1055 | CG | GLU | A | 141 | -19.442 | -7.962 | 16.345 | 1.00 | 16.15 |
| | ATOM | 1056 | CD | GLU | A | 141 | -18.579 | -9.035 | 15.701 | 1.00 | 18.73 |
| | ATOM | 1057 | OE1 | GLU | A | 141 | -19.093 | -9.712 | 14.788 | 1.00 | 20.83 |
| | ATOM | 1058 | OE2 | GLU | A | 141 | -17.396 | -9.190 | 16.097 | 1.00 | 19.56 |
| | ATOM | 1059 | C | GLU | A | 141 | -18.183 | -4.857 | 14.420 | 1.00 | 7.26 |
| | ATOM | 1060 | O | GLU | A | 141 | -17.936 | -5.120 | 13.258 | 1.00 | 6.79 |
| | ATOM | 1061 | N | SER | A | 142 | -18.543 | -3.637 | 14.815 | 1.00 | 7.82 |
| | ATOM | 1062 | CA | SER | A | 142 | -18.613 | -2.514 | 13.879 | 1.00 | 7.23 |
| | ATOM | 1063 | CB | SER | A | 142 | -19.015 | -1.231 | 14.616 | 1.00 | 8.19 |
| | ATOM | 1064 | OG | SER | A | 142 | -18.149 | -0.993 | 15.725 | 1.00 | 7.71 |
| | ATOM | 1065 | C | SER | A | 142 | -17.260 | -2.300 | 13.203 | 1.00 | 5.91 |
| | ATOM | 1066 | O | SER | A | 142 | -17.194 | -1.939 | 12.033 | 1.00 | 5.91 |
| | ATOM | 1067 | N | PHE | A | 143 | -16.181 | -2.532 | 13.945 | 1.00 | 5.73 |
| | ATOM | 1068 | CA | PHE | A | 143 | -14.841 | -2.353 | 13.400 | 1.00 | 5.63 |
| | ATOM | 1069 | CB | PHE | A | 143 | -13.800 | -2.245 | 14.521 | 1.00 | 5.11 |
| | ATOM | 1070 | CG | PHE | A | 143 | -12.435 | -1.852 | 14.036 | 1.00 | 3.97 |
| | ATOM | 1071 | CD1 | PHE | A | 143 | -12.115 | -0.514 | 13.860 | 1.00 | 2.76 |
| | ATOM | 1072 | CD2 | PHE | A | 143 | -11.468 | -2.822 | 13.771 | 1.00 | 2.00 |
| | ATOM | 1073 | CE1 | PHE | A | 143 | -10.843 | -0.138 | 13.436 | 1.00 | 3.44 |
| | ATOM | 1074 | CE2 | PHE | A | 143 | -10.203 | -2.458 | 13.349 | 1.00 | 3.53 |
| | ATOM | 1075 | CZ | PHE | A | 143 | -9.886 | -1.110 | 13.184 | 1.00 | 3.18 |
| | ATOM | 1076 | C | PHE | A | 143 | -14.507 | -3.506 | 12.460 | 1.00 | 6.01 |
| | ATOM | 1077 | O | PHE | A | 143 | -14.012 | -3.292 | 11.355 | 1.00 | 5.34 |
| | ATOM | 1078 | N | LEU | A | 144 | -14.804 | -4.726 | 12.891 | 1.00 | 7.20 |
| | ATOM | 1079 | CA | LEU | A | 144 | -14.539 | -5.909 | 12.070 | 1.00 | 8.00 |
| | ATOM | 1080 | CB | LEU | A | 144 | -15.002 | -7.176 | 12.809 | 1.00 | 9.33 |
| | ATOM | 1081 | CG | LEU | A | 144 | -14.691 | -8.525 | 12.151 | 1.00 | 10.59 |
| | ATOM | 1082 | CD1 | LEU | A | 144 | -13.194 | -8.661 | 11.890 | 1.00 | 10.40 |
| | ATOM | 1083 | CD2 | LEU | A | 144 | -15.177 | -9.644 | 13.050 | 1.00 | 9.64 |
| | ATOM | 1084 | C | LEU | A | 144 | -15.233 | -5.791 | 10.706 | 1.00 | 8.74 |
| | ATOM | 1085 | O | LEU | A | 144 | -14.640 | -6.077 | 9.661 | 1.00 | 8.65 |

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1086 | N | PHE | A | 145 | -16.481 | -5.321 | 10.730 | 1.00 | 9.71 |
| ATOM | 1087 | CA | PHE | A | 145 | -17.285 | -5.153 | 9.525 | 1.00 | 10.03 |
| ATOM | 1088 | CB | PHE | A | 145 | -18.721 | -5.624 | 9.789 | 1.00 | 9.79 |
| ATOM | 1089 | CG | PHE | A | 145 | -18.826 | -7.106 | 9.978 | 1.00 | 9.33 |
| ATOM | 1090 | CD1 | PHE | A | 145 | -18.931 | -7.949 | 8.877 | 1.00 | 9.14 |
| ATOM | 1091 | CD2 | PHE | A | 145 | -18.728 | -7.669 | 11.250 | 1.00 | 10.28 |
| ATOM | 1092 | CE1 | PHE | A | 145 | -18.925 | -9.326 | 9.037 | 1.00 | 8.42 |
| ATOM | 1093 | CE2 | PHE | A | 145 | -18.719 | -9.047 | 11.423 | 1.00 | 9.97 |
| ATOM | 1094 | CZ | PHE | A | 145 | -18.817 | -9.880 | 10.308 | 1.00 | 8.67 |
| ATOM | 1095 | C | PHE | A | 145 | -17.255 | -3.760 | 8.891 | 1.00 | 10.74 |
| ATOM | 1096 | O | PHE | A | 145 | -17.996 | -3.486 | 7.947 | 1.00 | 12.92 |
| ATOM | 1097 | N | TYR | A | 146 | -16.364 | -2.903 | 9.374 | 1.00 | 10.25 |
| ATOM | 1098 | CA | TYR | A | 146 | -16.211 | -1.552 | 8.840 | 1.00 | 10.24 |
| ATOM | 1099 | CB | TYR | A | 146 | -15.105 | -0.788 | 9.604 | 1.00 | 7.10 |
| ATOM | 1100 | CG | TYR | A | 146 | -14.647 | 0.469 | 8.896 | 1.00 | 6.36 |
| ATOM | 1101 | CD1 | TYR | A | 146 | -13.565 | 0.436 | 8.022 | 1.00 | 5.04 |
| ATOM | 1102 | CE1 | TYR | A | 146 | -13.185 | 1.565 | 7.317 | 1.00 | 4.47 |
| ATOM | 1103 | CD2 | TYR | A | 146 | -15.335 | 1.679 | 9.051 | 1.00 | 4.80 |
| ATOM | 1104 | CE2 | TYR | A | 146 | -14.952 | 2.806 | 8.354 | 1.00 | 2.25 |
| ATOM | 1105 | CZ | TYR | A | 146 | -13.883 | 2.737 | 7.498 | 1.00 | 2.89 |
| ATOM | 1106 | OH | TYR | A | 146 | -13.460 | 3.832 | 6.824 | 1.00 | 5.77 |
| ATOM | 1107 | C | TYR | A | 146 | -15.863 | -1.627 | 7.354 | 1.00 | 9.78 |
| ATOM | 1108 | O | TYR | A | 146 | -14.991 | -2.402 | 6.957 | 1.00 | 9.94 |
| ATOM | 1109 | N | ALA | A | 147 | -16.518 | -0.792 | 6.546 | 1.00 | 10.69 |
| ATOM | 1110 | CA | ALA | A | 147 | -16.274 | -0.766 | 5.105 | 1.00 | 9.95 |
| ATOM | 1111 | CB | ALA | A | 147 | -17.504 | -1.289 | 4.335 | 1.00 | 9.48 |
| ATOM | 1112 | C | ALA | A | 147 | -15.892 | 0.622 | 4.601 | 1.00 | 10.89 |
| ATOM | 1113 | O | ALA | A | 147 | -14.923 | 0.765 | 3.856 | 1.00 | 12.73 |
| ATOM | 1114 | N | GLY | A | 148 | -16.649 | 1.641 | 4.999 | 1.00 | 10.59 |
| ATOM | 1115 | CA | GLY | A | 148 | -16.354 | 2.986 | 4.535 | 1.00 | 11.28 |
| ATOM | 1116 | C | GLY | A | 148 | -16.821 | 4.094 | 5.451 | 1.00 | 10.19 |
| ATOM | 1117 | O | GLY | A | 148 | -17.563 | 3.862 | 6.409 | 1.00 | 11.41 |
| ATOM | 1118 | N | GLY | A | 149 | -16.337 | 5.303 | 5.180 | 1.00 | 11.89 |
| ATOM | 1119 | CA | GLY | A | 149 | -16.729 | 6.464 | 5.963 | 1.00 | 9.22 |
| ATOM | 1120 | C | GLY | A | 149 | -15.922 | 6.671 | 7.223 | 1.00 | 9.50 |
| ATOM | 1121 | O | GLY | A | 149 | -14.889 | 6.047 | 7.415 | 1.00 | 8.92 |
| ATOM | 1122 | N | ILE | A | 150 | -16.392 | 7.575 | 8.071 | 1.00 | 8.68 |

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1123 | CA | ILE | A | 150 | -15.730 | 7.860 | 9.321 | 1.00 | 8.49 |
| ATOM | 1124 | CB | ILE | A | 150 | -15.989 | 9.317 | 9.771 | 1.00 | 7.77 |
| ATOM | 1125 | CG2 | ILE | A | 150 | -15.408 | 9.569 | 11.161 | 1.00 | 7.93 |
| ATOM | 1126 | CG1 | ILE | A | 150 | -15.345 | 10.283 | 8.787 | 1.00 | 7.43 |
| ATOM | 1127 | CD1 | ILE | A | 150 | -15.440 | 11.716 | 9.233 | 1.00 | 9.23 |
| ATOM | 1128 | C | ILE | A | 150 | -16.253 | 6.866 | 10.350 | 1.00 | 8.25 |
| ATOM | 1129 | O | ILE | A | 150 | -17.461 | 6.803 | 10.599 | 1.00 | 8.91 |
| ATOM | 1130 | N | TYR | A | 151 | -15.352 | 6.037 | 10.873 | 1.00 | 6.97 |
| ATOM | 1131 | CA | TYR | A | 151 | -15.708 | 5.047 | 11.869 | 1.00 | 6.31 |
| ATOM | 1132 | CB | TYR | A | 151 | -14.559 | 4.038 | 12.087 | 1.00 | 4.18 |
| ATOM | 1133 | CG | TYR | A | 151 | -14.824 | 3.021 | 13.184 | 1.00 | 2.00 |
| ATOM | 1134 | CD1 | TYR | A | 151 | -15.687 | 1.943 | 12.964 | 1.00 | 2.93 |
| ATOM | 1135 | CE1 | TYR | A | 151 | -15.955 | 1.008 | 13.967 | 1.00 | 2.00 |
| ATOM | 1136 | CD2 | TYR | A | 151 | -14.225 | 3.140 | 14.449 | 1.00 | 2.00 |
| ATOM | 1137 | CE2 | TYR | A | 151 | -14.481 | 2.214 | 15.461 | 1.00 | 2.12 |
| ATOM | 1138 | CZ | TYR | A | 151 | -15.359 | 1.142 | 15.206 | 1.00 | 2.70 |
| ATOM | 1139 | OH | TYR | A | 151 | -15.654 | 0.216 | 16.179 | 1.00 | 3.04 |
| ATOM | 1140 | C | TYR | A | 151 | -16.016 | 5.729 | 13.181 | 1.00 | 6.36 |
| ATOM | 1141 | O | TYR | A | 151 | -15.200 | 6.482 | 13.704 | 1.00 | 7.11 |
| ATOM | 1142 | N | PHE | A | 152 | -17.193 | 5.458 | 13.717 | 1.00 | 6.45 |
| ATOM | 1143 | CA | PHE | A | 152 | -17.578 | 5.993 | 15.004 | 1.00 | 6.30 |
| ATOM | 1144 | CB | PHE | A | 152 | -18.461 | 7.243 | 14.880 | 1.00 | 6.56 |
| ATOM | 1145 | CG | PHE | A | 152 | -18.892 | 7.784 | 16.206 | 1.00 | 8.34 |
| ATOM | 1146 | CD1 | PHE | A | 152 | -17.972 | 8.380 | 17.057 | 1.00 | 9.05 |
| ATOM | 1147 | CD2 | PHE | A | 152 | -20.196 | 7.613 | 16.655 | 1.00 | 8.59 |
| ATOM | 1148 | CE1 | PHE | A | 152 | -18.349 | 8.784 | 18.330 | 1.00 | 8.82 |
| ATOM | 1149 | CE2 | PHE | A | 152 | -20.573 | 8.014 | 17.924 | 1.00 | 6.13 |
| ATOM | 1150 | CZ | PHE | A | 152 | -19.658 | 8.593 | 18.757 | 1.00 | 7.60 |
| ATOM | 1151 | C | PHE | A | 152 | -18.320 | 4.871 | 15.716 | 1.00 | 6.20 |
| ATOM | 1152 | O | PHE | A | 152 | -19.259 | 4.299 | 15.174 | 1.00 | 6.53 |
| ATOM | 1153 | N | GLU | A | 153 | -17.892 | 4.558 | 16.926 | 1.00 | 6.07 |
| ATOM | 1154 | CA | GLU | A | 153 | -18.492 | 3.491 | 17.704 | 1.00 | 6.66 |
| ATOM | 1155 | CB | GLU | A | 153 | -17.494 | 2.319 | 17.774 | 1.00 | 6.95 |
| ATOM | 1156 | CG | GLU | A | 153 | -17.840 | 1.151 | 18.702 | 1.00 | 7.94 |
| ATOM | 1157 | CD | GLU | A | 153 | -19.263 | 0.620 | 18.540 | 1.00 | 7.75 |
| ATOM | 1158 | OE1 | GLU | A | 153 | -19.594 | 0.045 | 17.500 | 1.00 | 7.60 |
| ATOM | 1159 | OE2 | GLU | A | 153 | -20.054 | 0.764 | 19.488 | 1.00 | 11.97 |

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1160 | C | GLU | A | 153 | -18.791 | 4.026 | 19.087 | 1.00 7.28 |
| ATOM | 1161 | O | GLU | A | 153 | -17.898 | 4.133 | 19.915 | 1.00 10.59 |
| ATOM | 1162 | N | PRO | A | 154 | -20.052 | 4.341 | 19.375 | 1.00 7.39 |
| ATOM | 1163 | CD | PRO | A | 154 | -21.217 | 4.180 | 18.491 | 1.00 8.01 |
| ATOM | 1164 | CA | PRO | A | 154 | -20.453 | 4.870 | 20.679 | 1.00 8.73 |
| ATOM | 1165 | CB | PRO | A | 154 | -21.974 | 4.997 | 20.537 | 1.00 9.35 |
| ATOM | 1166 | CG | PRO | A | 154 | -22.324 | 3.997 | 19.475 | 1.00 9.09 |
| ATOM | 1167 | C | PRO | A | 154 | -20.050 | 4.041 | 21.906 | 1.00 10.41 |
| ATOM | 1168 | O | PRO | A | 154 | -19.930 | 4.575 | 23.008 | 1.00 10.29 |
| ATOM | 1169 | N | ASP | A | 155 | -19.787 | 2.752 | 21.695 | 1.00 12.63 |
| ATOM | 1170 | CA | ASP | A | 155 | -19.401 | 1.838 | 22.772 | 1.00 14.09 |
| ATOM | 1171 | CB | ASP | A | 155 | -19.993 | 0.450 | 22.498 | 1.00 18.24 |
| ATOM | 1172 | CG | ASP | A | 155 | -20.572 | -0.203 | 23.740 | 1.00 22.25 |
| ATOM | 1173 | OD1 | ASP | A | 155 | -20.087 | 0.073 | 24.866 | 1.00 24.23 |
| ATOM | 1174 | OD2 | ASP | A | 155 | -21.515 | -1.011 | 23.583 | 1.00 23.87 |
| ATOM | 1175 | C | ASP | A | 155 | -17.886 | 1.718 | 22.945 | 1.00 12.31 |
| ATOM | 1176 | O | ASP | A | 155 | -17.409 | 0.985 | 23.820 | 1.00 11.49 |
| ATOM | 1177 | N | CYS | A | 156 | -17.138 | 2.448 | 22.124 | 1.00 11.10 |
| ATOM | 1178 | CA | CYS | A | 156 | -15.673 | 2.421 | 22.159 | 1.00 10.25 |
| ATOM | 1179 | C | CYS | A | 156 | -15.082 | 2.958 | 23.463 | 1.00 11.02 |
| ATOM | 1180 | O | CYS | A | 156 | -15.592 | 3.918 | 24.037 | 1.00 13.17 |
| ATOM | 1181 | CB | CYS | A | 156 | -15.103 | 3.204 | 20.981 | 1.00 9.79 |
| ATOM | 1182 | SG | CYS | A | 156 | -13.922 | 2.253 | 19.981 | 1.00 9.59 |
| ATOM | 1183 | N | SER | A | 157 | -13.977 | 2.357 | 23.891 | 1.00 9.16 |
| ATOM | 1184 | CA | SER | A | 157 | -13.286 | 2.741 | 25.114 | 1.00 9.33 |
| ATOM | 1185 | CB | SER | A | 157 | -12.870 | 1.495 | 25.897 | 1.00 9.13 |
| ATOM | 1186 | OG | SER | A | 157 | -12.026 | 1.833 | 26.989 | 1.00 11.98 |
| ATOM | 1187 | C | SER | A | 157 | -12.043 | 3.573 | 24.802 | 1.00 9.01 |
| ATOM | 1188 | O | SER | A | 157 | -11.311 | 3.280 | 23.851 | 1.00 7.33 |
| ATOM | 1189 | N | SER | A | 158 | -11.820 | 4.613 | 25.598 | 1.00 11.32 |
| ATOM | 1190 | CA | SER | A | 158 | -10.665 | 5.490 | 25.437 | 1.00 12.82 |
| ATOM | 1191 | CB | SER | A | 158 | -11.066 | 6.940 | 25.756 | 1.00 12.61 |
| ATOM | 1192 | OG | SER | A | 158 | -12.015 | 7.406 | 24.807 | 1.00 14.29 |
| ATOM | 1193 | C | SER | A | 158 | -9.526 | 5.051 | 26.352 | 1.00 13.31 |
| ATOM | 1194 | O | SER | A | 158 | -8.454 | 5.651 | 26.343 | 1.00 13.89 |
| ATOM | 1195 | N | GLU | A | 159 | -9.751 | 3.959 | 27.082 | 1.00 14.86 |
| ATOM | 1196 | CA | GLU | A | 159 | -8.784 | 3.420 | 28.047 | 1.00 17.99 |

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ATOM   1197  CB  GLU A 159     -9.376   3.507  29.472  1.00 21.62
ATOM   1198  CG  GLU A 159     -9.327   4.893  30.174  1.00 27.72
ATOM   1199  CD  GLU A 159    -10.044   6.040  29.431  1.00 31.08
ATOM   1200  OE1 GLU A 159    -11.217   5.881  29.015  1.00 33.32
ATOM   1201  OE2 GLU A 159     -9.431   7.128  29.286  1.00 33.60
ATOM   1202  C   GLU A 159     -8.336   1.968  27.783  1.00 17.27
ATOM   1203  O   GLU A 159     -7.237   1.568  28.177  1.00 15.65
ATOM   1204  N   ASP A 160     -9.201   1.173  27.158  1.00 17.33
ATOM   1205  CA  ASP A 160     -8.881  -0.224  26.879  1.00 16.78
ATOM   1206  CB  ASP A 160     -9.899  -1.163  27.529  1.00 19.87
ATOM   1207  CG  ASP A 160     -9.660  -1.329  29.020  1.00 22.08
ATOM   1208  OD1 ASP A 160    -10.537  -0.901  29.801  1.00 23.73
ATOM   1209  OD2 ASP A 160     -8.594  -1.870  29.416  1.00 24.26
ATOM   1210  C   ASP A 160     -8.691  -0.567  25.414  1.00 15.82
ATOM   1211  O   ASP A 160     -9.548  -1.190  24.770  1.00 15.21
ATOM   1212  N   MET A 161     -7.536  -0.155  24.911  1.00 12.42
ATOM   1213  CA  MET A 161     -7.122  -0.395  23.540  1.00 10.56
ATOM   1214  CB  MET A 161     -5.984   0.566  23.177  1.00  9.97
ATOM   1215  CG  MET A 161     -6.373   2.052  23.206  1.00  8.93
ATOM   1216  SD  MET A 161     -6.388   2.808  24.831  1.00  6.75
ATOM   1217  CE  MET A 161     -4.613   2.868  25.169  1.00  6.35
ATOM   1218  C   MET A 161     -6.629  -1.837  23.445  1.00  9.06
ATOM   1219  O   MET A 161     -6.045  -2.356  24.389  1.00  5.78
ATOM   1220  N   ASP A 162     -6.795  -2.448  22.276  1.00  9.89
ATOM   1221  CA  ASP A 162     -6.386  -3.849  22.086  1.00  9.12
ATOM   1222  CB  ASP A 162     -7.607  -4.773  22.327  1.00  9.68
ATOM   1223  CG  ASP A 162     -8.753  -4.538  21.324  1.00 10.19
ATOM   1224  OD1 ASP A 162     -9.690  -5.359  21.283  1.00 12.60
ATOM   1225  OD2 ASP A 162     -8.717  -3.557  20.560  1.00  9.29
ATOM   1226  C   ASP A 162     -5.780  -4.158  20.718  1.00  7.20
ATOM   1227  O   ASP A 162     -5.447  -5.302  20.419  1.00  7.80
ATOM   1228  N   HIS A 163     -5.594  -3.129  19.905  1.00  6.08
ATOM   1229  CA  HIS A 163     -5.101  -3.314  18.550  1.00  5.69
ATOM   1230  CB  HIS A 163     -6.319  -3.387  17.620  1.00  3.42
ATOM   1231  CG  HIS A 163     -5.996  -3.718  16.201  1.00  4.55
ATOM   1232  CD2 HIS A 163     -6.293  -3.070  15.050  1.00  4.77
ATOM   1233  ND1 HIS A 163     -5.272  -4.828  15.835  1.00  5.31
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ATOM   1234  CE1 HIS A 163      -5.128  -4.850  14.525  1.00  3.80
ATOM   1235  NE2 HIS A 163      -5.741  -3.796  14.024  1.00  4.91
ATOM   1236  C   HIS A 163      -4.177  -2.159  18.164  1.00  5.34
ATOM   1237  O   HIS A 163      -4.574  -1.001  18.192  1.00  5.40
ATOM   1238  N   GLY A 164      -2.943  -2.491  17.812  1.00  5.58
ATOM   1239  CA  GLY A 164      -1.972  -1.479  17.439  1.00  3.48
ATOM   1240  C   GLY A 164      -2.068  -1.253  15.954  1.00  3.74
ATOM   1241  O   GLY A 164      -2.004  -2.211  15.174  1.00  3.16
ATOM   1242  N   VAL A 165      -2.224   0.010  15.573  1.00  2.32
ATOM   1243  CA  VAL A 165      -2.365   0.410  14.182  1.00  2.00
ATOM   1244  CB  VAL A 165      -3.844   0.801  13.844  1.00  2.00
ATOM   1245  CG1 VAL A 165      -4.731  -0.468  13.780  1.00  2.00
ATOM   1246  CG2 VAL A 165      -4.397   1.772  14.881  1.00  2.00
ATOM   1247  C   VAL A 165      -1.403   1.557  13.889  1.00  2.00
ATOM   1248  O   VAL A 165      -0.541   1.864  14.704  1.00  3.95
ATOM   1249  N   LEU A 166      -1.540   2.185  12.729  1.00  2.00
ATOM   1250  CA  LEU A 166      -0.634   3.252  12.350  1.00  2.00
ATOM   1251  CB  LEU A 166       0.312   2.715  11.263  1.00  2.00
ATOM   1252  CG  LEU A 166       1.405   3.677  10.812  1.00  2.06
ATOM   1253  CD1 LEU A 166       2.468   3.784  11.906  1.00  2.00
ATOM   1254  CD2 LEU A 166       1.993   3.198   9.512  1.00  2.00
ATOM   1255  C   LEU A 166      -1.370   4.490  11.815  1.00  2.00
ATOM   1256  O   LEU A 166      -2.151   4.381  10.882  1.00  2.91
ATOM   1257  N   VAL A 167      -1.124   5.656  12.397  1.00  2.00
ATOM   1258  CA  VAL A 167      -1.742   6.881  11.911  1.00  2.07
ATOM   1259  CB  VAL A 167      -1.948   7.930  13.029  1.00  2.33
ATOM   1260  CG1 VAL A 167      -2.537   9.230  12.458  1.00  2.00
ATOM   1261  CG2 VAL A 167      -2.870   7.396  14.044  1.00  2.00
ATOM   1262  C   VAL A 167      -0.813   7.459  10.861  1.00  2.42
ATOM   1263  O   VAL A 167       0.343   7.764  11.149  1.00  4.10
ATOM   1264  N   VAL A 168      -1.302   7.556   9.631  1.00  2.00
ATOM   1265  CA  VAL A 168      -0.498   8.107   8.561  1.00  2.89
ATOM   1266  CB  VAL A 168      -0.455   7.187   7.288  1.00  2.89
ATOM   1267  CG1 VAL A 168      -0.099   5.746   7.665  1.00  2.00
ATOM   1268  CG2 VAL A 168      -1.760   7.246   6.501  1.00  2.49
ATOM   1269  C   VAL A 168      -0.985   9.515   8.193  1.00  2.09
ATOM   1270  O   VAL A 168      -0.454  10.139   7.284  1.00  2.00
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ATOM   1271  N   GLY A 169      -1.995  10.009   8.897  1.00  2.00
ATOM   1272  CA  GLY A 169      -2.487  11.330   8.575  1.00  2.00
ATOM   1273  C   GLY A 169      -3.819  11.615   9.207  1.00  3.02
ATOM   1274  O   GLY A 169      -4.263  10.874  10.087  1.00  2.26
ATOM   1275  N   TYR A 170      -4.442  12.711   8.779  1.00  4.13
ATOM   1276  CA  TYR A 170      -5.739  13.121   9.287  1.00  4.16
ATOM   1277  CB  TYR A 170      -5.613  13.859  10.631  1.00  7.05
ATOM   1278  CG  TYR A 170      -4.674  15.062  10.650  1.00  8.77
ATOM   1279  CD1 TYR A 170      -5.096  16.322  10.221  1.00  9.89
ATOM   1280  CE1 TYR A 170      -4.257  17.431  10.313  1.00  9.67
ATOM   1281  CD2 TYR A 170      -3.380  14.944  11.161  1.00  9.54
ATOM   1282  CE2 TYR A 170      -2.538  16.043  11.249  1.00 10.90
ATOM   1283  CZ  TYR A 170      -2.988  17.284  10.827  1.00 10.64
ATOM   1284  OH  TYR A 170      -2.167  18.367  10.977  1.00 11.05
ATOM   1285  C   TYR A 170      -6.426  13.994   8.263  1.00  5.39
ATOM   1286  O   TYR A 170      -5.820  14.420   7.262  1.00  4.57
ATOM   1287  N   GLY A 171      -7.703  14.244   8.489  1.00  4.36
ATOM   1288  CA  GLY A 171      -8.436  15.067   7.556  1.00  5.12
ATOM   1289  C   GLY A 171      -9.835  15.311   8.051  1.00  5.48
ATOM   1290  O   GLY A 171     -10.154  15.080   9.220  1.00  5.50
ATOM   1291  N   PHE A 172     -10.685  15.725   7.127  1.00  8.43
ATOM   1292  CA  PHE A 172     -12.073  16.028   7.437  1.00 12.21
ATOM   1293  CB  PHE A 172     -12.188  17.461   8.015  1.00 10.64
ATOM   1294  CG  PHE A 172     -11.753  18.511   7.058  1.00 12.04
ATOM   1295  CD1 PHE A 172     -12.674  19.079   6.166  1.00 12.73
ATOM   1296  CD2 PHE A 172     -10.400  18.811   6.913  1.00 10.22
ATOM   1297  CE1 PHE A 172     -12.241  19.911   5.127  1.00 13.64
ATOM   1298  CE2 PHE A 172      -9.961  19.631   5.892  1.00 10.76
ATOM   1299  CZ  PHE A 172     -10.875  20.183   4.989  1.00 11.62
ATOM   1300  C   PHE A 172     -12.869  15.898   6.138  1.00 12.68
ATOM   1301  O   PHE A 172     -12.305  15.964   5.029  1.00 12.32
ATOM   1302  N   GLU A 173     -14.164  15.649   6.275  1.00 16.06
ATOM   1303  CA  GLU A 173     -15.032  15.532   5.111  1.00 19.68
ATOM   1304  CB  GLU A 173     -15.958  14.310   5.238  1.00 21.86
ATOM   1305  CG  GLU A 173     -15.252  12.943   5.244  1.00 25.42
ATOM   1306  CD  GLU A 173     -16.219  11.738   5.208  1.00 27.43
ATOM   1307  OE1 GLU A 173     -17.371  11.830   5.721  1.00 26.18
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ATOM   1308  OE2 GLU A 173     -15.806  10.683   4.664  1.00 29.03
ATOM   1309  C   GLU A 173     -15.861  16.814   5.034  1.00 19.87
ATOM   1310  O   GLU A 173     -16.475  17.209   6.019  1.00 19.21
ATOM   1311  N   SER A 174     -15.852  17.473   3.879  1.00 21.76
ATOM   1312  CA  SER A 174     -16.611  18.709   3.685  1.00 23.39
ATOM   1313  CB  SER A 174     -16.263  19.326   2.336  1.00 24.50
ATOM   1314  OG  SER A 174     -15.900  20.691   2.504  1.00 29.61
ATOM   1315  C   SER A 174     -18.129  18.530   3.798  1.00 23.13
ATOM   1316  O   SER A 174     -18.731  17.741   3.066  1.00 24.67
ATOM   1316  OH  SER A 174     -18.731  19.741   3.066  1.00 24.67
ATOM   1317  N   ASN B 179     -18.343  16.440  13.685  1.00 29.23
ATOM   1318  CA  ASN B 179     -18.080  15.003  13.614  1.00 28.13
ATOM   1319  CB  ASN B 179     -19.293  14.240  14.147  1.00 29.81
ATOM   1320  CG  ASN B 179     -19.614  14.606  15.594  1.00 30.79
ATOM   1321  OD1 ASN B 179     -18.796  15.226  16.289  1.00 30.85
ATOM   1322  ND2 ASN B 179     -20.804  14.226  16.057  1.00 31.47
ATOM   1323  C   ASN B 179     -17.791  14.671  12.158  1.00 26.17
ATOM   1324  O   ASN B 179     -18.385  13.764  11.553  1.00 27.58
ATOM   1325  N   ASN B 180     -16.898  15.479  11.593  1.00 23.23
ATOM   1326  CA  ASN B 180     -16.475  15.365  10.204  1.00 18.57
ATOM   1327  CB  ASN B 180     -16.935  16.598   9.420  1.00 18.84
ATOM   1328  CG  ASN B 180     -16.057  17.815   9.680  1.00 17.60
ATOM   1329  OD1 ASN B 180     -15.578  18.027  10.796  1.00 19.00
ATOM   1330  ND2 ASN B 180     -15.818  18.597   8.646  1.00 18.32
ATOM   1331  C   ASN B 180     -14.948  15.239  10.098  1.00 15.32
ATOM   1332  O   ASN B 180     -14.395  15.224   8.993  1.00 14.06
ATOM   1333  N   LYS B 181     -14.262  15.211  11.232  1.00 11.94
ATOM   1334  CA  LYS B 181     -12.821  15.063  11.189  1.00 11.71
ATOM   1335  CB  LYS B 181     -12.155  16.013  12.188  1.00 11.39
ATOM   1336  CG  LYS B 181     -12.080  17.434  11.640  1.00 12.51
ATOM   1337  CD  LYS B 181     -11.385  18.400  12.587  1.00 10.42
ATOM   1338  CE  LYS B 181     -12.228  18.659  13.784  1.00 11.13
ATOM   1339  NZ  LYS B 181     -11.566  19.675  14.640  1.00 13.87
ATOM   1340  C   LYS B 181     -12.439  13.592  11.423  1.00 10.20
ATOM   1341  O   LYS B 181     -13.179  12.838  12.066  1.00  6.89
ATOM   1342  N   TYR B 182     -11.291  13.187  10.883  1.00 11.29
ATOM   1343  CA  TYR B 182     -10.816  11.809  11.030  1.00  9.68
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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | ATOM | 1344 | CB | TYR | B | 182 | -11.373 | 10.924 | 9.896 | 1.00 | 8.59 |
| | ATOM | 1345 | CG | TYR | B | 182 | -10.889 | 11.299 | 8.512 | 1.00 | 8.36 |
| | ATOM | 1346 | CD1 | TYR | B | 182 | -11.657 | 12.118 | 7.686 | 1.00 | 8.98 |
| | ATOM | 1347 | CE1 | TYR | B | 182 | -11.217 | 12.491 | 6.424 | 1.00 | 8.31 |
| 5 | ATOM | 1348 | CD2 | TYR | B | 182 | -9.657 | 10.858 | 8.034 | 1.00 | 9.50 |
| | ATOM | 1349 | CE2 | TYR | B | 182 | -9.193 | 11.237 | 6.770 | 1.00 | 8.86 |
| | ATOM | 1350 | CZ | TYR | B | 182 | -9.986 | 12.058 | 5.968 | 1.00 | 10.80 |
| | ATOM | 1351 | OH | TYR | B | 182 | -9.553 | 12.454 | 4.711 | 1.00 | 12.63 |
| | ATOM | 1352 | C | TYR | B | 182 | -9.298 | 11.693 | 11.013 | 1.00 | 8.23 |
| 10 | ATOM | 1353 | O | TYR | B | 182 | -8.597 | 12.588 | 10.531 | 1.00 | 8.51 |
| | ATOM | 1354 | N | TRP | B | 183 | -8.827 | 10.541 | 11.483 | 1.00 | 6.74 |
| | ATOM | 1355 | CA | TRP | B | 183 | -7.413 | 10.174 | 11.492 | 1.00 | 5.15 |
| | ATOM | 1356 | CB | TRP | B | 183 | -6.997 | 9.471 | 12.810 | 1.00 | 3.98 |
| | ATOM | 1357 | CG | TRP | B | 183 | -6.971 | 10.324 | 14.044 | 1.00 | 2.37 |
| 15 | ATOM | 1358 | CD2 | TRP | B | 183 | -6.030 | 11.363 | 14.352 | 1.00 | 2.00 |
| | ATOM | 1359 | CE2 | TRP | B | 183 | -6.408 | 11.918 | 15.591 | 1.00 | 2.08 |
| | ATOM | 1360 | CE3 | TRP | B | 183 | -4.902 | 11.878 | 13.690 | 1.00 | 2.00 |
| | ATOM | 1361 | CD1 | TRP | B | 183 | -7.857 | 10.284 | 15.093 | 1.00 | 2.00 |
| | ATOM | 1362 | NE1 | TRP | B | 183 | -7.523 | 11.240 | 16.024 | 1.00 | 2.18 |
| 20 | ATOM | 1363 | CZ2 | TRP | B | 183 | -5.702 | 12.971 | 16.190 | 1.00 | 2.00 |
| | ATOM | 1364 | CZ3 | TRP | B | 183 | -4.200 | 12.922 | 14.287 | 1.00 | 2.00 |
| | ATOM | 1365 | CH2 | TRP | B | 183 | -4.609 | 13.456 | 15.529 | 1.00 | 2.00 |
| | ATOM | 1366 | C | TRP | B | 183 | -7.331 | 9.141 | 10.381 | 1.00 | 4.37 |
| | ATOM | 1367 | O | TRP | B | 183 | -8.206 | 8.290 | 10.260 | 1.00 | 5.30 |
| 25 | ATOM | 1368 | N | LEU | B | 184 | -6.336 | 9.256 | 9.522 | 1.00 | 4.89 |
| | ATOM | 1369 | CA | LEU | B | 184 | -6.148 | 8.282 | 8.467 | 1.00 | 5.71 |
| | ATOM | 1370 | CB | LEU | B | 184 | -5.398 | 8.914 | 7.296 | 1.00 | 6.57 |
| | ATOM | 1371 | CG | LEU | B | 184 | -5.366 | 8.064 | 6.027 | 1.00 | 8.89 |
| | ATOM | 1372 | CD1 | LEU | B | 184 | -6.765 | 7.619 | 5.659 | 1.00 | 10.53 |
| 30 | ATOM | 1373 | CD2 | LEU | B | 184 | -4.756 | 8.862 | 4.904 | 1.00 | 10.66 |
| | ATOM | 1374 | C | LEU | B | 184 | -5.322 | 7.166 | 9.150 | 1.00 | 6.28 |
| | ATOM | 1375 | O | LEU | B | 184 | -4.180 | 7.386 | 9.551 | 1.00 | 5.46 |
| | ATOM | 1376 | N | VAL | B | 185 | -5.935 | 5.995 | 9.314 | 1.00 | 6.48 |
| | ATOM | 1377 | CA | VAL | B | 185 | -5.318 | 4.861 | 10.003 | 1.00 | 4.83 |
| 35 | ATOM | 1378 | CB | VAL | B | 185 | -6.154 | 4.518 | 11.262 | 1.00 | 5.57 |
| | ATOM | 1379 | CG1 | VAL | B | 185 | -5.682 | 3.208 | 11.916 | 1.00 | 6.15 |
| | ATOM | 1380 | CG2 | VAL | B | 185 | -6.095 | 5.690 | 12.255 | 1.00 | 4.05 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | ATOM | 1381 | C | VAL | B | 185 | -5.070 | 3.597 | 9.160 | 1.00 | 5.60 |
| | ATOM | 1382 | O | VAL | B | 185 | -5.996 | 3.024 | 8.583 | 1.00 | 2.61 |
| | ATOM | 1383 | N | LYS | B | 186 | -3.792 | 3.212 | 9.067 | 1.00 | 5.93 |
| | ATOM | 1384 | CA | LYS | B | 186 | -3.360 | 2.013 | 8.348 | 1.00 | 5.03 |
| 5 | ATOM | 1385 | CB | LYS | B | 186 | -1.898 | 2.145 | 7.910 | 1.00 | 2.00 |
| | ATOM | 1386 | CG | LYS | B | 186 | -1.412 | 0.974 | 7.058 | 1.00 | 3.08 |
| | ATOM | 1387 | CD | LYS | B | 186 | 0.083 | 1.045 | 6.833 | 1.00 | 2.00 |
| | ATOM | 1388 | CE | LYS | B | 186 | 0.497 | 0.145 | 5.694 | 1.00 | 2.00 |
| | ATOM | 1389 | NZ | LYS | B | 186 | 1.960 | -0.032 | 5.588 | 1.00 | 2.08 |
| 10 | ATOM | 1390 | C | LYS | B | 186 | -3.504 | 0.788 | 9.265 | 1.00 | 3.70 |
| | ATOM | 1391 | O | LYS | B | 186 | -2.961 | 0.766 | 10.368 | 1.00 | 3.08 |
| | ATOM | 1392 | N | ASN | B | 187 | -4.244 | -0.221 | 8.806 | 1.00 | 4.50 |
| | ATOM | 1393 | CA | ASN | B | 187 | -4.448 | -1.453 | 9.584 | 1.00 | 3.91 |
| | ATOM | 1394 | CB | ASN | B | 187 | -5.938 | -1.863 | 9.554 | 1.00 | 3.32 |
| 15 | ATOM | 1395 | CG | ASN | B | 187 | -6.311 | -2.843 | 10.645 | 1.00 | 2.76 |
| | ATOM | 1396 | OD1 | ASN | B | 187 | -5.470 | -3.254 | 11.437 | 1.00 | 3.97 |
| | ATOM | 1397 | ND2 | ASN | B | 187 | -7.592 | -3.189 | 10.723 | 1.00 | 2.00 |
| | ATOM | 1398 | C | ASN | B | 187 | -3.565 | -2.548 | 8.959 | 1.00 | 3.91 |
| | ATOM | 1399 | O | ASN | B | 187 | -2.906 | -2.320 | 7.930 | 1.00 | 5.02 |
| 20 | ATOM | 1400 | N | SER | B | 188 | -3.499 | -3.704 | 9.609 | 1.00 | 3.14 |
| | ATOM | 1401 | CA | SER | B | 188 | -2.715 | -4.822 | 9.106 | 1.00 | 3.31 |
| | ATOM | 1402 | CB | SER | B | 188 | -1.553 | -5.142 | 10.042 | 1.00 | 2.00 |
| | ATOM | 1403 | OG | SER | B | 188 | -1.970 | -5.238 | 11.391 | 1.00 | 2.00 |
| | ATOM | 1404 | C | SER | B | 188 | -3.607 | -6.042 | 8.905 | 1.00 | 3.75 |
| 25 | ATOM | 1405 | O | SER | B | 188 | -3.233 | -7.160 | 9.245 | 1.00 | 3.49 |
| | ATOM | 1406 | N | TRP | B | 189 | -4.778 | -5.808 | 8.323 | 1.00 | 5.44 |
| | ATOM | 1407 | CA | TRP | B | 189 | -5.745 | -6.864 | 8.036 | 1.00 | 6.30 |
| | ATOM | 1408 | CB | TRP | B | 189 | -7.086 | -6.568 | 8.694 | 1.00 | 5.78 |
| | ATOM | 1409 | CG | TRP | B | 189 | -7.075 | -6.721 | 10.165 | 1.00 | 5.36 |
| 30 | ATOM | 1410 | CD2 | TRP | B | 189 | -8.131 | -6.373 | 11.049 | 1.00 | 4.80 |
| | ATOM | 1411 | CE2 | TRP | B | 189 | -7.685 | -6.637 | 12.360 | 1.00 | 4.52 |
| | ATOM | 1412 | CE3 | TRP | B | 189 | -9.422 | -5.854 | 10.861 | 1.00 | 4.80 |
| | ATOM | 1413 | CD1 | TRP | B | 189 | -6.053 | -7.184 | 10.947 | 1.00 | 5.31 |
| | ATOM | 1414 | NE1 | TRP | B | 189 | -6.411 | -7.133 | 12.271 | 1.00 | 3.77 |
| 35 | ATOM | 1415 | CZ2 | TRP | B | 189 | -8.485 | -6.396 | 13.481 | 1.00 | 6.20 |
| | ATOM | 1416 | CZ3 | TRP | B | 189 | -10.213 | -5.617 | 11.963 | 1.00 | 3.93 |
| | ATOM | 1417 | CH2 | TRP | B | 189 | -9.744 | -5.886 | 13.263 | 1.00 | 6.61 |

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ATOM   1418  C   TRP B 189      -5.940  -7.053   6.533  1.00  6.24
ATOM   1419  O   TRP B 189      -6.985  -7.530   6.078  1.00  8.03
ATOM   1420  N   GLY B 190      -4.914  -6.698   5.770  1.00  5.57
ATOM   1421  CA  GLY B 190      -4.968  -6.857   4.336  1.00  7.76
ATOM   1422  C   GLY B 190      -5.709  -5.708   3.710  1.00  9.19
ATOM   1423  O   GLY B 190      -6.386  -4.955   4.410  1.00  9.35
ATOM   1424  N   GLU B 191      -5.599  -5.572   2.396  1.00 11.99
ATOM   1425  CA  GLU B 191      -6.265  -4.477   1.729  1.00 15.41
ATOM   1426  CB  GLU B 191      -5.491  -3.992   0.494  1.00 18.10
ATOM   1427  CG  GLU B 191      -5.680  -4.772  -0.778  1.00 22.38
ATOM   1428  CD  GLU B 191      -5.576  -3.886  -2.012  1.00 24.80
ATOM   1429  OE1 GLU B 191      -4.495  -3.292  -2.239  1.00 25.76
ATOM   1430  OE2 GLU B 191      -6.586  -3.777  -2.750  1.00 25.33
ATOM   1431  C   GLU B 191      -7.740  -4.671   1.422  1.00 16.08
ATOM   1432  O   GLU B 191      -8.378  -3.741   0.963  1.00 18.21
ATOM   1433  N   GLU B 192      -8.309  -5.838   1.716  1.00 16.39
ATOM   1434  CA  GLU B 192      -9.731  -6.042   1.439  1.00 17.58
ATOM   1435  CB  GLU B 192     -10.018  -7.461   0.939  1.00 21.48
ATOM   1436  CG  GLU B 192     -10.005  -7.608  -0.600  1.00 24.93
ATOM   1437  CD  GLU B 192      -8.651  -7.314  -1.229  1.00 27.46
TOM    1438  OE1 GLU B 192      -7.663  -8.018  -0.884  1.00 29.01
ATOM   1439  OE2 GLU B 192      -8.578  -6.387  -2.076  1.00 28.64
ATOM   1440  C   GLU B 192     -10.622  -5.677   2.619  1.00 15.65
ATOM   1441  O   GLU B 192     -11.842  -5.779   2.540  1.00 17.05
ATOM   1442  N   TRP B 193     -10.000  -5.321   3.735  1.00 12.72
ATOM   1443  CA  TRP B 193     -10.726  -4.890   4.915  1.00 10.26
ATOM   1444  CB  TRP B 193      -9.945  -5.205   6.195  1.00  9.01
ATOM   1445  CG  TRP B 193     -10.609  -4.662   7.418  1.00  6.29
ATOM   1446  CD2 TRP B 193     -10.359  -3.395   8.043  1.00  6.14
ATOM   1447  CE2 TRP B 193     -11.254  -3.282   9.126  1.00  5.42
ATOM   1448  CE3 TRP B 193      -9.465  -2.342   7.791  1.00  5.54
ATOM   1449  CD1 TRP B 193     -11.610  -5.250   8.133  1.00  6.47
ATOM   1450  NE1 TRP B 193     -12.002  -4.428   9.155  1.00  7.53
ATOM   1451  CZ2 TRP B 193     -11.286  -2.166   9.956  1.00  5.40
ATOM   1452  CZ3 TRP B 193      -9.493  -1.234   8.617  1.00  2.49
ATOM   1453  CH2 TRP B 193     -10.395  -1.152   9.683  1.00  4.22
ATOM   1454  C   TRP B 193     -10.808  -3.369   4.772  1.00 10.85
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| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | ATOM | 1455 | O | TRP | B | 193 | -9.881 | -2.753 | 4.238 | 1.00 11.56 |
| | ATOM | 1456 | N | GLY | B | 194 | -11.881 | -2.773 | 5.288 | 1.00 11.54 |
| | ATOM | 1457 | CA | GLY | B | 194 | -12.047 | -1.334 | 5.232 | 1.00 9.53 |
| | ATOM | 1458 | C | GLY | B | 194 | -11.857 | -0.749 | 3.859 | 1.00 10.38 |
| 5 | ATOM | 1459 | O | GLY | B | 194 | -12.201 | -1.373 | 2.845 | 1.00 12.08 |
| | ATOM | 1460 | N | MET | B | 195 | -11.281 | 0.443 | 3.819 | 1.00 10.12 |
| | ATOM | 1461 | CA | MET | B | 195 | -11.051 | 1.131 | 2.561 | 1.00 10.17 |
| | ATOM | 1462 | CB | MET | B | 195 | -11.234 | 2.636 | 2.749 | 1.00 12.77 |
| | ATOM | 1463 | CG | MET | B | 195 | -12.577 | 3.011 | 3.368 | 1.00 14.51 |
| 10 | ATOM | 1464 | SD | MET | B | 195 | -12.818 | 4.797 | 3.503 | 1.00 15.17 |
| | ATOM | 1465 | CE | MET | B | 195 | -13.257 | 5.170 | 1.846 | 1.00 12.95 |
| | ATOM | 1466 | C | MET | B | 195 | -9.650 | 0.845 | 2.095 | 1.00 9.98 |
| | ATOM | 1467 | O | MET | B | 195 | -8.725 | 1.596 | 2.400 | 1.00 12.23 |
| | ATOM | 1468 | N | GLY | B | 196 | -9.481 | -0.244 | 1.350 | 1.00 10.11 |
| 15 | ATOM | 1469 | CA | GLY | B | 196 | -8.158 | -0.607 | 0.873 | 1.00 7.24 |
| | ATOM | 1470 | C | GLY | B | 196 | -7.198 | -0.863 | 2.020 | 1.00 5.18 |
| | ATOM | 1471 | O | GLY | B | 196 | -6.006 | -0.613 | 1.910 | 1.00 6.22 |
| | ATOM | 1472 | N | GLY | B | 197 | -7.733 | -1.327 | 3.138 | 1.00 5.69 |
| | ATOM | 1473 | CA | GLY | B | 197 | -6.912 | -1.612 | 4.297 | 1.00 6.35 |
| 20 | ATOM | 1474 | C | GLY | B | 197 | -6.801 | -0.492 | 5.310 | 1.00 5.93 |
| | ATOM | 1475 | O | GLY | B | 197 | -6.172 | -0.666 | 6.349 | 1.00 8.00 |
| | ATOM | 1476 | N | TYR | B | 198 | -7.397 | 0.655 | 5.001 | 1.00 6.76 |
| | ATOM | 1477 | CA | TYR | B | 198 | -7.387 | 1.826 | 5.877 | 1.00 4.21 |
| | ATOM | 1478 | CB | TYR | B | 198 | -7.034 | 3.096 | 5.085 | 1.00 3.49 |
| 25 | ATOM | 1479 | CG | TYR | B | 198 | -5.574 | 3.218 | 4.759 | 1.00 2.98 |
| | ATOM | 1480 | CD1 | TYR | B | 198 | -4.749 | 4.060 | 5.500 | 1.00 2.00 |
| | ATOM | 1481 | CE1 | TYR | B | 198 | -3.372 | 4.090 | 5.287 | 1.00 2.00 |
| | ATOM | 1482 | CD2 | TYR | B | 198 | -4.997 | 2.412 | 3.784 | 1.00 3.11 |
| | ATOM | 1483 | CE2 | TYR | B | 198 | -3.629 | 2.432 | 3.561 | 1.00 2.79 |
| 30 | ATOM | 1484 | CZ | TYR | B | 198 | -2.815 | 3.270 | 4.315 | 1.00 2.98 |
| | ATOM | 1485 | OH | TYR | B | 198 | -1.450 | 3.278 | 4.077 | 1.00 3.39 |
| | ATOM | 1486 | C | TYR | B | 198 | -8.752 | 2.030 | 6.489 | 1.00 4.93 |
| | ATOM | 1487 | O | TYR | B | 198 | -9.758 | 1.503 | 6.003 | 1.00 5.90 |
| | ATOM | 1488 | N | VAL | B | 199 | -8.777 | 2.830 | 7.547 | 1.00 4.85 |
| 35 | ATOM | 1489 | CA | VAL | B | 199 | -9.998 | 3.172 | 8.250 | 1.00 4.01 |
| | ATOM | 1490 | CB | VAL | B | 199 | -10.297 | 2.192 | 9.470 | 1.00 3.06 |
| | ATOM | 1491 | CG1 | VAL | B | 199 | -9.041 | 1.972 | 10.349 | 1.00 2.46 |

| | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|
| | ATOM | 1492 | CG2 | VAL | B | 199 | -11.471 | 2.709 | 10.312 | 1.00 | 2.00 |
| | ATOM | 1493 | C | VAL | B | 199 | -9.854 | 4.637 | 8.703 | 1.00 | 5.20 |
| | ATOM | 1494 | O | VAL | B | 199 | -8.766 | 5.072 | 9.113 | 1.00 | 5.29 |
| | ATOM | 1495 | N | LYS | B | 200 | -10.901 | 5.422 | 8.456 | 1.00 | 5.99 |
| 5 | ATOM | 1496 | CA | LYS | B | 200 | -10.945 | 6.824 | 8.865 | 1.00 | 3.79 |
| | ATOM | 1497 | CB | LYS | B | 200 | -11.784 | 7.648 | 7.889 | 1.00 | 4.53 |
| | ATOM | 1498 | CG | LYS | B | 200 | -11.142 | 7.778 | 6.513 | 1.00 | 4.39 |
| | ATOM | 1499 | CD | LYS | B | 200 | -11.760 | 8.851 | 5.602 | 1.00 | 5.37 |
| | ATOM | 1500 | CE | LYS | B | 200 | -13.096 | 8.479 | 5.057 | 1.00 | 6.22 |
| 10 | ATOM | 1501 | NZ | LYS | B | 200 | -13.314 | 9.154 | 3.734 | 1.00 | 8.43 |
| | ATOM | 1502 | C | LYS | B | 200 | -11.588 | 6.813 | 10.229 | 1.00 | 4.61 |
| | ATOM | 1503 | O | LYS | B | 200 | -12.790 | 6.645 | 10.334 | 1.00 | 6.47 |
| | ATOM | 1504 | N | MET | B | 201 | -10.761 | 6.899 | 11.272 | 1.00 | 5.90 |
| | ATOM | 1505 | CA | MET | B | 201 | -11.201 | 6.880 | 12.668 | 1.00 | 4.43 |
| 15 | ATOM | 1506 | CB | MET | B | 201 | -10.044 | 6.385 | 13.553 | 1.00 | 6.85 |
| | ATOM | 1507 | CG | MET | B | 201 | -9.616 | 4.921 | 13.344 | 1.00 | 7.98 |
| | ATOM | 1508 | SD | MET | B | 201 | -10.856 | 3.793 | 13.965 | 1.00 | 8.47 |
| | ATOM | 1509 | CE | MET | B | 201 | -10.568 | 3.867 | 15.739 | 1.00 | 7.39 |
| | ATOM | 1510 | C | MET | B | 201 | -11.625 | 8.276 | 13.131 | 1.00 | 3.89 |
| 20 | ATOM | 1511 | O | MET | B | 201 | -10.873 | 9.222 | 12.971 | 1.00 | 3.07 |
| | ATOM | 1512 | N | ALA | B | 202 | -12.803 | 8.393 | 13.739 | 1.00 | 5.48 |
| | ATOM | 1513 | CA | ALA | B | 202 | -13.316 | 9.677 | 14.237 | 1.00 | 6.98 |
| | ATOM | 1514 | CB | ALA | B | 202 | -14.556 | 9.438 | 15.120 | 1.00 | 6.14 |
| | ATOM | 1515 | C | ALA | B | 202 | -12.262 | 10.477 | 15.021 | 1.00 | 7.19 |
| 25 | ATOM | 1516 | O | ALA | B | 202 | -11.737 | 10.009 | 16.036 | 1.00 | 8.35 |
| | ATOM | 1517 | N | LYS | B | 203 | -11.948 | 11.672 | 14.539 | 1.00 | 6.08 |
| | ATOM | 1518 | CA | LYS | B | 203 | -10.962 | 12.542 | 15.173 | 1.00 | 3.97 |
| | ATOM | 1519 | CB | LYS | B | 203 | -9.991 | 13.058 | 14.109 | 1.00 | 3.43 |
| | ATOM | 1520 | CG | LYS | B | 203 | -8.975 | 14.096 | 14.571 | 1.00 | 4.08 |
| 30 | ATOM | 1521 | CD | LYS | B | 203 | -7.969 | 14.367 | 13.483 | 1.00 | 2.00 |
| | ATOM | 1522 | CE | LYS | B | 203 | -7.065 | 15.504 | 13.866 | 1.00 | 3.41 |
| | ATOM | 1523 | NZ | LYS | B | 203 | -7.795 | 16.808 | 13.845 | 1.00 | 3.63 |
| | ATOM | 1524 | C | LYS | B | 203 | -11.611 | 13.712 | 15.911 | 1.00 | 4.66 |
| | ATOM | 1525 | O | LYS | B | 203 | -12.626 | 14.277 | 15.462 | 1.00 | 5.34 |
| 35 | ATOM | 1526 | N | ASP | B | 204 | -11.023 | 14.033 | 17.058 | 1.00 | 5.46 |
| | ATOM | 1527 | CA | ASP | B | 204 | -11.452 | 15.112 | 17.938 | 1.00 | 8.48 |
| | ATOM | 1528 | CB | ASP | B | 204 | -11.312 | 16.469 | 17.243 | 1.00 | 7.66 |

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ATOM   1529  CG  ASP B 204     -9.875  16.785  16.879  1.00  5.97
ATOM   1530  OD1 ASP B 204     -8.983  16.543  17.720  1.00  6.13
ATOM   1531  OD2 ASP B 204     -9.630  17.246  15.746  1.00  6.01
ATOM   1532  C   ASP B 204    -12.856  14.908  18.483  1.00 11.09
ATOM   1533  O   ASP B 204    -13.639  15.853  18.609  1.00 12.16
ATOM   1534  N   ARG B 205    -13.155  13.658  18.830  1.00 10.89
ATOM   1535  CA  ARG B 205    -14.445  13.293  19.386  1.00  8.86
ATOM   1536  CB  ARG B 205    -15.189  12.392  18.418  1.00  9.96
ATOM   1537  CG  ARG B 205    -15.660  13.120  17.170  1.00  8.84
ATOM   1538  CD  ARG B 205    -16.979  12.543  16.735  1.00 11.03
ATOM   1539  NE  ARG B 205    -17.925  12.587  17.853  1.00 12.78
ATOM   1540  CZ  ARG B 205    -19.136  12.044  17.847  1.00 12.72
ATOM   1541  NH1 ARG B 205    -19.578  11.393  16.779  1.00 14.34
ATOM   1542  NH2 ARG B 205    -19.919  12.183  18.903  1.00 13.91
ATOM   1543  C   ARG B 205    -14.167  12.581  20.691  1.00 10.06
ATOM   1544  O   ARG B 205    -14.461  11.391  20.848  1.00  9.66
ATOM   1545  N   ALA B 206    -13.520  13.323  21.590  1.00  7.99
ATOM   1546  CA  ALA B 206    -13.118  12.871  22.922  1.00  9.48
ATOM   1547  CB  ALA B 206    -14.334  12.704  23.835  1.00  9.13
ATOM   1548  C   ALA B 206    -12.214  11.630  22.976  1.00  8.23
ATOM   1549  O   ALA B 206    -12.425  10.747  23.793  1.00  8.74
ATOM   1550  N   ASN B 207    -11.168  11.618  22.147  1.00  7.13
ATOM   1551  CA  ASN B 207    -10.191  10.521  22.096  1.00  5.29
ATOM   1552  CB  ASN B 207     -9.439  10.401  23.430  1.00  4.29
ATOM   1553  CG  ASN B 207     -8.238   9.470  23.346  1.00  3.56
ATOM   1554  OD1 ASN B 207     -7.783   9.117  22.252  1.00  5.32
ATOM   1555  ND2 ASN B 207     -7.711   9.088  24.495  1.00  3.67
ATOM   1556  C   ASN B 207    -10.902   9.214  21.756  1.00  4.96
ATOM   1557  O   ASN B 207    -10.786   8.202  22.456  1.00  4.62
ATOM   1558  N   HIS B 208    -11.638   9.256  20.658  1.00  5.63
ATOM   1559  CA  HIS B 208    -12.413   8.117  20.198  1.00  5.79
ATOM   1560  CB  HIS B 208    -13.133   8.468  18.894  1.00  5.93
ATOM   1561  CG  HIS B 208    -14.188   7.485  18.515  1.00  6.32
ATOM   1562  CD2 HIS B 208    -14.330   6.707  17.418  1.00  6.76
ATOM   1563  ND1 HIS B 208    -15.239   7.175  19.346  1.00  7.15
ATOM   1564  CE1 HIS B 208    -15.982   6.241  18.783  1.00  7.14
ATOM   1565  NE2 HIS B 208    -15.452   5.939  17.613  1.00  7.63
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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1566 | C | HIS | B | 208 | -11.584 | 6.843 | 20.019 | 1.00 | 7.12 |
| ATOM | 1567 | O | HIS | B | 208 | -10.643 | 6.792 | 19.181 | 1.00 | 5.72 |
| ATOM | 1568 | N | CYS | B | 209 | -11.988 | 5.814 | 20.774 | 1.00 | 7.20 |
| ATOM | 1569 | CA | CYS | B | 209 | -11.346 | 4.495 | 20.781 | 1.00 | 7.10 |
| ATOM | 1570 | C | CYS | B | 209 | -9.894 | 4.547 | 21.312 | 1.00 | 5.42 |
| ATOM | 1571 | O | CYS | B | 209 | -9.070 | 3.681 | 20.990 | 1.00 | 4.32 |
| ATOM | 1572 | CB | CYS | B | 209 | -11.412 | 3.857 | 19.385 | 1.00 | 8.32 |
| ATOM | 1573 | SG | CYS | B | 209 | -13.091 | 3.602 | 18.713 | 1.00 | 10.94 |
| ATOM | 1574 | N | GLY | B | 210 | -9.603 | 5.572 | 22.119 | 1.00 | 3.19 |
| ATOM | 1575 | CA | GLY | B | 210 | -8.283 | 5.758 | 22.712 | 1.00 | 2.87 |
| ATOM | 1576 | C | GLY | B | 210 | -7.129 | 5.913 | 21.742 | 1.00 | 3.31 |
| ATOM | 1577 | O | GLY | B | 210 | -5.973 | 5.573 | 22.061 | 1.00 | 7.40 |
| ATOM | 1578 | N | ILE | B | 211 | -7.413 | 6.451 | 20.570 | 1.00 | 2.00 |
| ATOM | 1579 | CA | ILE | B | 211 | -6.387 | 6.612 | 19.553 | 1.00 | 2.00 |
| ATOM | 1580 | CB | ILE | B | 211 | -6.981 | 7.148 | 18.250 | 1.00 | 2.48 |
| ATOM | 1581 | CG2 | ILE | B | 211 | -7.504 | 8.578 | 18.437 | 1.00 | 3.27 |
| ATOM | 1582 | CG1 | ILE | B | 211 | -5.942 | 7.033 | 17.135 | 1.00 | 2.07 |
| ATOM | 1583 | CD1 | ILE | B | 211 | -6.495 | 7.020 | 15.792 | 1.00 | 2.62 |
| ATOM | 1584 | C | ILE | B | 211 | -5.176 | 7.433 | 19.990 | 1.00 | 3.39 |
| ATOM | 1585 | O | ILE | B | 211 | -4.064 | 7.203 | 19.523 | 1.00 | 4.21 |
| ATOM | 1586 | N | ALA | B | 212 | -5.360 | 8.324 | 20.951 | 1.00 | 2.80 |
| ATOM | 1587 | CA | ALA | B | 212 | -4.253 | 9.142 | 21.433 | 1.00 | 3.27 |
| ATOM | 1588 | CB | ALA | B | 212 | -4.661 | 10.618 | 21.437 | 1.00 | 4.12 |
| ATOM | 1589 | C | ALA | B | 212 | -3.760 | 8.726 | 22.822 | 1.00 | 2.81 |
| ATOM | 1590 | O | ALA | B | 212 | -2.908 | 9.402 | 23.394 | 1.00 | 3.98 |
| ATOM | 1591 | N | SER | B | 213 | -4.253 | 7.603 | 23.346 | 1.00 | 2.50 |
| ATOM | 1592 | CA | SER | B | 213 | -3.869 | 7.141 | 24.685 | 1.00 | 3.65 |
| ATOM | 1593 | CB | SER | B | 213 | -4.984 | 6.284 | 25.313 | 1.00 | 4.01 |
| ATOM | 1594 | OG | SER | B | 213 | -6.229 | 6.976 | 25.350 | 1.00 | 5.80 |
| ATOM | 1595 | C | SER | B | 213 | -2.532 | 6.404 | 24.800 | 1.00 | 2.77 |
| ATOM | 1596 | O | SER | B | 213 | -1.979 | 6.311 | 25.886 | 1.00 | 5.92 |
| ATOM | 1597 | N | ALA | B | 214 | -2.043 | 5.849 | 23.696 | 1.00 | 6.22 |
| ATOM | 1598 | CA | ALA | B | 214 | -0.775 | 5.122 | 23.680 | 1.00 | 6.26 |
| ATOM | 1599 | CB | ALA | B | 214 | -0.996 | 3.633 | 23.957 | 1.00 | 6.33 |
| ATOM | 1600 | C | ALA | B | 214 | -0.116 | 5.315 | 22.327 | 1.00 | 5.15 |
| ATOM | 1601 | O | ALA | B | 214 | 0.117 | 4.349 | 21.591 | 1.00 | 5.92 |
| ATOM | 1602 | N | ALA | B | 215 | 0.154 | 6.573 | 21.985 | 1.00 | 3.16 |

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|---|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1603 | CA | ALA | B | 215 | 0.780 | 6.901 | 20.707 | 1.00 | 3.49 |
| ATOM | 1604 | CB | ALA | B | 215 | 0.124 | 8.189 | 20.091 | 1.00 | 2.00 |
| ATOM | 1605 | C | ALA | B | 215 | 2.289 | 7.085 | 20.886 | 1.00 | 3.15 |
| ATOM | 1606 | O | ALA | B | 215 | 2.754 | 7.576 | 21.931 | 1.00 | 3.84 |
| ATOM | 1607 | N | SER | B | 216 | 3.056 | 6.680 | 19.882 | 1.00 | 2.80 |
| ATOM | 1608 | CA | SER | B | 216 | 4.510 | 6.800 | 19.943 | 1.00 | 2.95 |
| ATOM | 1609 | CB | SER | B | 216 | 5.080 | 5.835 | 20.992 | 1.00 | 5.18 |
| ATOM | 1610 | OG | SER | B | 216 | 4.914 | 4.487 | 20.572 | 1.00 | 6.13 |
| ATOM | 1611 | C | SER | B | 216 | 5.152 | 6.525 | 18.575 | 1.00 | 3.03 |
| ATOM | 1612 | O | SER | B | 216 | 4.490 | 6.051 | 17.640 | 1.00 | 3.02 |
| ATOM | 1613 | N | TYR | B | 217 | 6.437 | 6.855 | 18.469 | 1.00 | 3.25 |
| ATOM | 1614 | CA | TYR | B | 217 | 7.214 | 6.644 | 17.251 | 1.00 | 3.81 |
| ATOM | 1615 | CB | TYR | B | 217 | 7.101 | 7.853 | 16.297 | 1.00 | 4.94 |
| ATOM | 1616 | CG | TYR | B | 217 | 7.657 | 9.164 | 16.829 | 1.00 | 5.35 |
| ATOM | 1617 | CD1 | TYR | B | 217 | 8.954 | 9.559 | 16.536 | 1.00 | 5.88 |
| ATOM | 1618 | CE1 | TYR | B | 217 | 9.455 | 10.791 | 16.955 | 1.00 | 6.10 |
| ATOM | 1619 | CD2 | TYR | B | 217 | 6.865 | 10.036 | 17.568 | 1.00 | 6.74 |
| ATOM | 1620 | CE2 | TYR | B | 217 | 7.360 | 11.284 | 17.994 | 1.00 | 7.90 |
| ATOM | 1621 | CZ | TYR | B | 217 | 8.657 | 11.646 | 17.676 | 1.00 | 7.27 |
| ATOM | 1622 | OH | TYR | B | 217 | 9.153 | 12.865 | 18.075 | 1.00 | 9.53 |
| ATOM | 1623 | C | TYR | B | 217 | 8.677 | 6.400 | 17.662 | 1.00 | 3.37 |
| ATOM | 1624 | O | TYR | B | 217 | 9.079 | 6.757 | 18.777 | 1.00 | 2.04 |
| ATOM | 1625 | N | PRO | B | 218 | 9.475 | 5.746 | 16.791 | 1.00 | 5.38 |
| ATOM | 1626 | CD | PRO | B | 218 | 9.086 | 4.997 | 15.572 | 1.00 | 2.00 |
| ATOM | 1627 | CA | PRO | B | 218 | 10.883 | 5.489 | 17.136 | 1.00 | 4.81 |
| ATOM | 1628 | CB | PRO | B | 218 | 11.204 | 4.223 | 16.329 | 1.00 | 2.00 |
| ATOM | 1629 | CG | PRO | B | 218 | 10.419 | 4.417 | 15.094 | 1.00 | 2.00 |
| ATOM | 1630 | C | PRO | B | 218 | 11.810 | 6.669 | 16.763 | 1.00 | 5.05 |
| ATOM | 1631 | O | PRO | B | 218 | 11.553 | 7.366 | 15.791 | 1.00 | 5.60 |
| ATOM | 1632 | N | THR | B | 219 | 12.831 | 6.929 | 17.579 | 1.00 | 6.63 |
| ATOM | 1633 | CA | THR | B | 219 | 13.781 | 8.005 | 17.297 | 1.00 | 9.58 |
| ATOM | 1634 | CB | THR | B | 219 | 14.396 | 8.645 | 18.582 | 1.00 | 10.22 |
| ATOM | 1635 | OG1 | THR | B | 219 | 15.062 | 7.652 | 19.366 | 1.00 | 11.19 |
| ATOM | 1636 | CG2 | THR | B | 219 | 13.320 | 9.293 | 19.434 | 1.00 | 10.92 |
| ATOM | 1637 | C | THR | B | 219 | 14.888 | 7.429 | 16.438 | 1.00 | 11.99 |
| ATOM | 1638 | O | THR | B | 219 | 15.419 | 6.350 | 16.714 | 1.00 | 11.40 |
| ATOM | 1639 | N | VAL | B | 220 | 15.191 | 8.101 | 15.344 | 1.00 | 15.02 |

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|---|---|---|---|---|---|---|---|---|---|
| ATOM | 1640 | CA | VAL | B | 220 | 16.235 | 7.625 | 14.466 | 1.00 16.04 |
| ATOM | 1641 | CB | VAL | B | 220 | 15.672 | 7.471 | 13.031 | 1.00 16.05 |
| ATOM | 1642 | CG1 | VAL | B | 220 | 16.733 | 7.103 | 12.089 | 1.00 17.27 |
| ATOM | 1643 | CG2 | VAL | B | 220 | 14.637 | 6.353 | 13.010 | 1.00 14.61 |
| ATOM | 1644 | C | VAL | B | 220 | 17.454 | 8.570 | 14.599 | 1.00 19.22 |
| ATOM | 1645 | O | VAL | B | 220 | 18.620 | 8.098 | 14.498 | 1.00 21.47 |
| ATOM | 1646 | OH | VAL | B | 220 | 17.243 | 9.755 | 14.954 | 1.00 18.51 |
| ATOM | 1647 | OH2 | WAT | C | 400 | 1.715 | -0.341 | 10.220 | 1.00 4.25 |
| ATOM | 1648 | OH2 | WAT | C | 401 | 7.097 | 7.224 | 11.030 | 1.00 2.00 |
| ATOM | 1649 | OH2 | WAT | C | 402 | -10.695 | 7.378 | 16.639 | 1.00 5.94 |
| ATOM | 1650 | OH2 | WAT | C | 403 | 2.737 | 3.013 | 20.821 | 1.00 5.69 |
| ATOM | 1651 | OH2 | WAT | C | 404 | 4.712 | -2.112 | 7.932 | 1.00 4.54 |
| ATOM | 1652 | OH2 | WAT | C | 405 | -0.335 | -2.968 | 7.131 | 1.00 2.00 |
| ATOM | 1653 | OH2 | WAT | C | 406 | -13.889 | -1.040 | 17.915 | 1.00 3.20 |
| ATOM | 1654 | OH2 | WAT | C | 407 | -5.874 | 17.220 | 22.788 | 1.00 7.23 |
| ATOM | 1655 | OH2 | WAT | C | 408 | -8.649 | 16.659 | 11.052 | 1.00 7.00 |
| ATOM | 1656 | OH2 | WAT | C | 409 | 5.217 | 4.237 | 7.361 | 1.00 2.00 |
| ATOM | 1657 | OH2 | WAT | C | 410 | 4.460 | 1.690 | 6.263 | 1.00 2.45 |
| ATOM | 1658 | OH2 | WAT | C | 411 | 12.655 | 9.649 | 14.739 | 1.00 10.53 |
| ATOM | 1659 | OH2 | WAT | C | 412 | 17.802 | -10.437 | 17.933 | 1.00 9.17 |
| ATOM | 1660 | OH2 | WAT | C | 413 | -17.578 | -5.887 | 21.444 | 1.00 8.88 |
| ATOM | 1661 | OH2 | WAT | C | 414 | -3.197 | 5.183 | 20.980 | 1.00 7.65 |
| ATOM | 1662 | OH2 | WAT | C | 415 | -5.965 | -3.631 | 6.935 | 1.00 5.92 |
| ATOM | 1663 | OH2 | WAT | C | 416 | 12.786 | 1.123 | 6.736 | 1.00 5.33 |
| ATOM | 1664 | OH2 | WAT | C | 417 | 3.012 | 16.347 | 20.074 | 1.00 6.15 |
| ATOM | 1665 | OH2 | WAT | C | 418 | -6.541 | 17.076 | 17.084 | 1.00 4.69 |
| ATOM | 1666 | OH2 | WAT | C | 419 | 8.324 | -10.560 | 8.482 | 1.00 4.57 |
| ATOM | 1667 | OH2 | WAT | C | 420 | -15.621 | -11.150 | 15.846 | 1.00 12.03 |
| ATOM | 1668 | OH2 | WAT | C | 421 | -11.693 | 11.210 | 18.286 | 1.00 2.91 |
| ATOM | 1669 | OH2 | WAT | C | 422 | -0.401 | 8.726 | 24.177 | 1.00 8.52 |
| ATOM | 1670 | OH2 | WAT | C | 423 | -0.681 | -0.811 | 11.002 | 1.00 2.50 |
| ATOM | 1671 | OH2 | WAT | C | 424 | 2.152 | -1.861 | 7.987 | 1.00 7.69 |
| ATOM | 1672 | OH2 | WAT | C | 425 | 10.844 | -17.495 | 11.881 | 1.00 24.05 |
| ATOM | 1673 | OH2 | WAT | C | 426 | 4.113 | 6.208 | 0.742 | 1.00 9.50 |
| ATOM | 1674 | OH2 | WAT | C | 427 | -0.361 | 18.287 | 4.743 | 1.00 21.23 |
| ATOM | 1675 | OH2 | WAT | C | 428 | -2.237 | 20.526 | 17.810 | 1.00 16.66 |
| ATOM | 1676 | OH2 | WAT | C | 429 | -19.138 | -6.191 | 19.225 | 1.00 7.57 |

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ATOM   1677  OH2 WAT C 430      19.473 -14.562  15.685  1.00 11.49
ATOM   1678  OH2 WAT C 431      -1.376  -2.848  12.708  1.00  3.21
ATOM   1679  OH2 WAT C 432       3.284   3.606  24.573  1.00  9.31
ATOM   1680  OH2 WAT C 433     -14.786  15.166  14.179  1.00 14.71
ATOM   1681  OH2 WAT C 434      12.094  -5.678   2.193  1.00 11.37
ATOM   1682  OH2 WAT C 435       6.466 -11.420   4.246  1.00  6.71
ATOM   1683  OH2 WAT C 436      22.706  -5.931  15.160  1.00  8.12
ATOM   1684  OH2 WAT C 437      -8.611  19.110  10.002  1.00  9.78
ATOM   1685  OH2 WAT C 438       0.738  15.034   3.641  1.00 20.62
ATOM   1686  OH2 WAT C 439       4.124  -9.086   6.384  1.00 14.29
ATOM   1687  OH2 WAT C 440     -13.887  -3.607   2.668  1.00 13.17
ATOM   1688  OH2 WAT C 441      -7.572  14.126  23.703  1.00 18.38
ATOM   1689  OH2 WAT C 442       0.874   7.459  26.362  1.00 22.12
ATOM   1690  OH2 WAT C 443       9.305 -14.700  20.411  1.00 20.46
ATOM   1691  OH2 WAT C 444      -8.955  15.927   4.448  1.00 25.82
ATOM   1692  OH2 WAT C 445      11.930 -13.702  21.523  1.00 10.86
ATOM   1693  OH2 WAT C 446       3.469 -16.357  23.297  1.00 19.39
ATOM   1694  OH2 WAT C 447      11.878   3.079   5.063  1.00  8.26
ATOM   1695  OH2 WAT C 448      -3.082   3.376   0.174  1.00 11.22
ATOM   1696  OH2 WAT C 449      -4.375   0.291   0.313  1.00  7.70
ATOM   1697  OH2 WAT C 450       4.771  14.939  -2.264  1.00 11.11
ATOM   1698  OH2 WAT C 451      15.349   1.340   6.121  1.00 14.46
ATOM   1699  OH2 WAT C 452      -0.319   1.922   2.215  1.00  6.91
ATOM   1700  OH2 WAT C 453      15.061 -15.434   4.049  1.00 21.29
ATOM   1701  OH2 WAT C 454     -15.574   9.174  21.509  1.00 19.68
ATOM   1702  OH2 WAT C 455      -5.683 -18.497  22.276  1.00  7.98
ATOM   1703  OH2 WAT C 456      16.054   3.526   4.535  1.00 15.78
ATOM   1704  OH2 WAT C 457       1.796  -9.826   5.952  1.00 15.52
ATOM   1705  OH2 WAT C 458       7.900 -11.446  20.651  1.00  9.56
ATOM   1706  OH2 WAT C 459     -15.694  12.658  13.651  1.00 15.95
ATOM   1707  OH2 WAT C 460     -18.800   4.491   8.685  1.00 30.26
ATOM   1708  OH2 WAT C 461       3.842  -3.870   2.301  1.00  5.98
ATOM   1709  OH2 WAT C 462      -1.911  -0.828  -0.023  1.00 11.85
ATOM   1710  OH2 WAT C 463     -19.071   4.290  11.811  1.00  9.95
ATOM   1711  OH2 WAT C 464     -10.861  -2.452   0.116  1.00 19.11
ATOM   1712  OH2 WAT C 465      -9.801  14.751  22.263  1.00 15.42
ATOM   1713  OH2 WAT C 466      -7.905   6.223   1.616  1.00 30.93
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ATOM   1714  OH2 WAT C 467      18.856   4.715  11.980  1.00 10.43
ATOM   1715  OH2 WAT C 468       4.553  17.830  24.004  1.00 19.36
ATOM   1716  OH2 WAT C 469     -22.103  -6.169  18.782  1.00 26.20
ATOM   1717  OH2 WAT C 470      22.883  -2.193  20.022  1.00 27.05
ATOM   1718  OH2 WAT C 471      -8.283  18.361  22.060  1.00 14.94
ATOM   1719  OH2 WAT C 472     -19.067  -4.655  23.491  1.00 12.52
ATOM   1720  OH2 WAT C 473     -25.358   3.482  20.935  1.00 18.60
ATOM   1721  OH2 WAT C 474       3.113   1.129  25.678  1.00 16.37
ATOM   1722  OH2 WAT C 475     -14.114  19.680  -0.525  1.00 19.49
ATOM   1723  OH2 WAT C 476       7.483  15.405  -1.684  1.00 20.28
ATOM   1724  OH2 WAT C 477       2.890  14.130  29.288  1.00 22.65
ATOM   1725  OH2 WAT C 478     -24.545  -8.477  18.440  1.00 22.79
ATOM   1726  OH2 WAT C 479      23.711  -7.909  16.612  1.00 26.08
ATOM   1727  OH2 WAT C 480      11.306   4.954  -1.712  1.00 18.71
ATOM   1728  OH2 WAT C 481      13.249   5.572  24.427  1.00 11.66
ATOM   1729  OH2 WAT C 482      14.941   3.560  24.925  1.00 18.00
ATOM   1730  OH2 WAT C 483      19.849   9.786  12.745  1.00 21.86
ATOM   1731  OH2 WAT C 484      -7.714  15.740  26.319  1.00 19.77
ATOM   1732  OH2 WAT C 485      18.128 -14.939  19.458  1.00 17.22
ATOM   1733  OH2 WAT C 486     -21.893  -4.075  14.601  1.00 21.40
ATOM   1734  OH2 WAT C 487      -2.211  22.607  20.592  1.00 27.68
ATOM   1735  OH2 WAT C 488      -9.940  17.323  20.067  1.00 15.74
ATOM   1736  OH2 WAT C 489       2.969  17.859   7.635  1.00 17.12
ATOM   1737  OH2 WAT C 490      -7.798  -7.724  -4.389  1.00 13.80
ATOM   1738  OH2 WAT C 491      21.839  -2.359  11.757  1.00 21.04
ATOM   1739  OH2 WAT C 492       3.610   1.069  22.604  1.00 11.34
ATOM   1740  OH2 WAT C 493      10.695  -2.690   0.512  1.00 21.14
ATOM   1741  OH2 WAT C 494      15.726 -17.968  19.611  1.00 16.41
ATOM   1742  OH2 WAT C 495      18.038 -14.823   8.893  1.00 22.45
ATOM   1743  OH2 WAT C 496     -19.607  -0.615  11.547  1.00 16.65
ATOM   1744  OH2 WAT C 497       2.915  15.247   5.332  1.00 15.60
ATOM   1745  OH2 WAT C 498      19.132 -12.808  17.530  1.00 13.34
ATOM   1746  OH2 WAT C 499      -2.344 -16.737   9.713  1.00 16.66
ATOM   1747  OH2 WAT C 500     -18.639   0.788   7.355  1.00 15.66
ATOM   1748  OH2 WAT C 501       0.462  15.302  -2.725  1.00 14.82
ATOM   1749  OH2 WAT C 502      -7.398  20.029  12.052  1.00 26.98
ATOM   1750  OH2 WAT C 503      15.757 -11.340  29.166  1.00 11.53
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ATOM   1751  OH2 WAT C 504      19.014   0.690   5.325  1.00 22.02
ATOM   1752  OH2 WAT C 505      16.120 -13.057  20.864  1.00 15.98
ATOM   1753  OH2 WAT C 506      -6.380  18.090  29.315  1.00 16.80
ATOM   1754  OH2 WAT C 507      14.293 -15.012  21.072  1.00 13.45
ATOM   1755  OH2 WAT C 508       9.526 -19.735  19.933  1.00 21.58
ATOM   1756  OH2 WAT C 509     -12.325  16.124  21.846  1.00 20.83
ATOM   1757  OH2 WAT C 510      15.864   7.749  25.554  1.00 11.44
ATOM   1758  OH2 WAT C 511      20.012  -0.457  24.073  1.00 17.87
ATOM   1759  OH2 WAT C 512       2.459   6.458  24.433  1.00 20.00
ATOM   1760  OH2 WAT C 513      -3.245  -7.574  17.264  1.00 20.00
ATOM   1761  OH2 WAT C 514      -2.009  -5.446  -5.665  1.00 20.00
ATOM   1762  OH2 WAT C 515      11.141  -3.191  26.733  1.00 20.00
ATOM   1763  OH2 WAT C 516      -1.734  -4.445  21.459  1.00 20.00
ATOM   1764  OH2 WAT C 517      -7.062  19.554  16.658  1.00 20.00
ATOM   1765  OH2 WAT C 518      10.312  -0.626  26.447  1.00 20.00
ATOM   1766  OH2 WAT C 519     -12.539  -5.135  28.522  1.00 20.00
ATOM   1767  OH2 WAT C 520      17.357  -8.676  23.160  1.00 20.00
ATOM   1768  OH2 WAT C 521       1.704  17.298  -2.824  1.00 20.00
ATOM   1769  OH2 WAT C 522     -24.997   6.317  22.486  1.00 20.00
ATOM   1770  OH2 WAT C 523      21.437   6.317  22.486  1.00 20.00
ATOM   1771  OH2 WAT C 524      11.336  16.240   9.222  1.00 20.00
ATOM   1772  OH2 WAT C 525      13.648  -3.524  28.036  1.00 20.00
ATOM   1773  OH2 WAT C 526      19.248 -10.257  26.167  1.00 20.00
ATOM   1774  OH2 WAT C 527     -22.056  -6.157  23.245  1.00 20.00
ATOM   1775  OH2 WAT C 528      24.378  -6.157  23.245  1.00 20.00
ATOM   1776  OH2 WAT C 529       3.398 -16.519  20.213  1.00 20.00
ATOM   1777  OH2 WAT C 530      -0.867  -2.050  22.075  1.00 20.00
ATOM   1778  OH2 WAT C 531      13.363 -12.892  28.748  1.00 20.00
ATOM   1779  OH2 WAT C 532      15.134 -16.191   7.553  1.00 20.00
ATOM   1780  OH2 WAT C 533      -2.778  -7.172  20.885  1.00 20.00
ATOM   1781  OH2 WAT C 534      -5.662  -6.615  -5.903  1.00 20.00
ATOM   1782  OH2 WAT C 535      18.366   2.686   3.326  1.00 20.00
ATOM   1783  OH2 WAT C 536      -1.839  15.842  -4.199  1.00 20.00
ATOM   1784  OH2 WAT C 537       8.606   5.745  -1.225  1.00 20.00
ATOM   1785  OH2 WAT C 538       4.084  16.971  -1.150  1.00 20.00
ATOM   1786  OH2 WAT C 539      -9.310 -12.146   0.259  1.00 20.00
ATOM   1787  OH2 WAT C 540     -13.659   5.332  27.584  1.00 20.00
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ATOM   1788  OH2 WAT C 541     -13.793  20.379   9.540  1.00 20.00
ATOM   1789  OH2 WAT C 542     -20.284  -3.453  17.374  1.00 20.00
ATOM   1790  OH2 WAT C 543       9.337  13.701   8.362  1.00 20.00
ATOM   1791  OH2 WAT C 544      -9.440 -10.243  -4.503  1.00 20.00
ATOM   1792  OH2 WAT C 545      12.473   0.613  27.161  1.00 20.00
ATOM   1793  OH2 WAT C 546      16.546 -17.419   8.428  1.00 20.00
ATOM   1794  OH2 WAT C 547      -1.129  -4.481  -0.369  1.00 20.00
ATOM   1795  OH2 WAT C 548      12.028 -16.285  22.590  1.00 20.00
ATOM   1796  OH2 WAT C 549     -10.803  20.596   9.099  1.00 20.00
ATOM   1797  OH2 WAT C 550     -21.302   6.052  25.675  1.00 20.00
ATOM   1798  OH2 WAT C 551      20.665   2.849  18.416  1.00 20.00
ATOM   1799  OH2 WAT C 552       8.171 -13.093  23.401  1.00 20.00
ATOM   1800  OH2 WAT C 553      10.372  -2.692  29.515  1.00 20.00
ATOM   1801  OH2 WAT C 554      10.863 -15.981   7.960  1.00 20.00
ATOM   1802  OH2 WAT C 555      -2.252  -5.584  24.473  1.00 20.00
ATOM   1803  OH2 WAT C 556       6.457  -5.032   2.210  1.00 20.00
ATOM   1804  OH2 WAT C 557     -11.210  17.326   2.413  1.00 20.00
END
```

## Example 5

### Assay of Inhibition of Cathepsin L Activity

Potential drugs may be tested for inhibition of Cathepsin L activity as follows. Briefly, Cathepsin L (19 pM final as determined by active site titration using E-64, Barrett et al., 1981, Methods in Enzymology, 80: 535) is added to 750 µL of assay buffer consisting of 340 nM sodium acetate - 60 mM acetic acid (pH 5.5), 4 mM disodium EDTA, and 8 mM DTT. Peptides were added at concentrations ranging from on to 35 µM. After a 6 minute incubation at 25°C, 1500 uL of 0.1% Brij 35 was added and the reaction started with 5.0 µM Z-Phe-Arg-NMec(AMC) (AMC is aminomethylcoumarin). The fluorescence of the free aminomethylcoumarin is measured in a fluorimeter at excitation of 370 nm and an emission at 432 nm over a 6 minute time period. Fluorescence was converted to µM AMC released by using a standard curve generated by plotting µM AMC vs. fluorescence, and plotted vs. time. In order to calculate the velocities, a linear least squares analysis is performed over the initial part of the data. The $IC_{50}$ values are

determined from Dixon plots of the form V-/V+ (velocity without compound/velocity with compound) vs. compound concentration.

**Example 6**

**Assay of inhibition of proteoglycan degradation**

Cathepsins B and L have been found to degrade cartilage components, causing the degradation of associated proteoglycans (Maciewicz and Wotton, Biomedica Biochimica Acta, 50, 561-4, 1991). Previous results by the same researchers indicated that these enzymes are found in active form in the synovial fluid of arthritic patients. The conclusion drawn was that cysteine proteinases play a role in the etiology of arthritis.

Cartilage degradation can be induced by the *in vivo* injection of IL-1 into the joint capsule of rabbits, and the administration of a large serine protease inhibitor PN-1 (43 KD) can ameliorate this degradation (Stevens et al., Agents and Actions, Supplements , 39, 173-7, 1993). It has been found that low molecular weight synthetic peptide metalloproteinase inhibitor can prevent the breakdown of proteoglycan within articular cartilage in vitro. (Andrews et al., Agents and Actions, 37, 147-54, 1992). Certain cysteine endopeptidase inactivators were found to inhibit IL-1 stimulated structural cartilage proteoglycan degradation. E64 and Ep475, broad-spectrum cysteine protease inhibitors) did not work at 100 μM concentrations. However lipophilic derivatives inhibited at 10 μM to 1 μM concentrations. (Buttle et al., Biochemical Journal, 281, 175-7, 1992). Compounds can be tested for the ability to inhibit articular cartilage proteoglycan degradation, as measured by proteoglycan release after IL-1 stimulation.

The assay system used for testing the peptides for inhibitory activity of proteoglycan release is a micro organ culture assay (MOCA). Papain; cetyl pyridinium chloride and chondroitin sulfate type C is purchased from Sigma Chemical Co. (St. Louis, MO). Interleukin 1 alpha is purchased from Collaborative Research. ABCase, chrondroitinase, ABC lyase, and keratanase is obtained from ICI. $Na^{35}SO_4$ is purchased from NEN.

Articular cartilage explants from calf knee joints are maintained in culture in DMEM medium containing 20 μCi/ml $Na\ ^{35}SO_4$ for 48 hours for the incorporation of label

into newly synthesized proteoglycan (PG). The radiolabelled medium is then removed, the radiolabelled explants washed 3 x 30 ml cold DMEM and placed into a 96 well plate with or without IL-1 (Interleukin-1 alpha, 50 U/ml) and various concentrations of test compound. The explants are incubated first for 24 hours in the presence of IL-1 in order to ensure initiation of IL-1 induced auto-catalysis prior to the addition of various metalloprotease inhibitors for an additional 72 hours.

The newly synthesized radiolabelled proteoglycans released during the cultivation period are subjected to enzymatic digestion with papain. Briefly, an aliquot of 150 µl of medium from the original culture volume (300 µl) was incubated with 100 µl of papain (3 ml/ml) for 2 hours at 65°C. A 50 µl aliquot of the papain digested material containing radiolabelled $^{35}SO_4$ -gag (glycosaminoglycans, mucopolysaccharide) is incubated with 100 µl of cetylpyridinium chloride (cpc, 4% cpc + 40 nM $NaSO_4$) plus cold chondroitin sulfate standard (30 µl of 2.5 mg/ml solution). The samples are placed on ice for 60 minutes, and the radiolabelled gags are precipitated and collected on a 96 well plate harvester (MACH2, TOMTEC, Orange, CT) glass fiber filter. The filter is dried and counted after addition of 10 mls of scintillation cocktail (scintillant).

**SEQUENCE LISTING**

(1) GENERAL INFORMATION:

(i) APPLICANT:
(A) NAME: Zeneca Limited
(B) STREET: 15 Stanhope Gate
(C) CITY: London
(E) COUNTRY: United Kingdom
(F) POSTAL CODE (ZIP): W1Y 6LN
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(ii) TITLE OF INVENTION: Protein

(iii) NUMBER OF SEQUENCES: 8

(iv) COMPUTER READABLE FORM:
(A) MEDIUM TYPE: Floppy disk
(B) COMPUTER: IBM PC compatible
(C) OPERATING SYSTEM: PC-DOS/MS-DOS
(D) SOFTWARE: PatentIn Release #1.0, Version #1.30 (EPO)

(vi) PRIOR APPLICATION DATA:
(A) APPLICATION NUMBER: GB 9522660.1
(B) FILING DATE: 04-NOV-1995

(2) INFORMATION FOR SEQ ID NO: 1:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 1:

GCAGTAAGAT ATGAATCCTA CACT 24

(2) INFORMATION FOR SEQ ID NO: 2:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 24 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 2:

CATCACCGTC CACAGCTCAC ACAG 24

(2) INFORMATION FOR SEQ ID NO: 3:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 33 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 3:

GATGACCATG GCGACTCTAA CATTTGATCA CAG 33

(2) INFORMATION FOR SEQ ID NO: 4:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 29 base pairs

(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 4:

CTGCCTGAAT TCTTCACTGG TCATGTCTC 29

(2) INFORMATION FOR SEQ ID NO: 5:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 30 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 5:

CTATCCATAT GAGGCAACAG AAGAATCCTG 30

(2) INFORMATION FOR SEQ ID NO: 6:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 59 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: other nucleic acid

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 6:

GACAAGCTTG AATTCTTATT AGTGATGGTG ATGGTGGTGC ACAGTGGGGT AGCTGGCTG 59

(2) INFORMATION FOR SEQ ID NO: 7:

(i) SEQUENCE CHARACTERISTICS:
(A) LENGTH: 1575 base pairs
(B) TYPE: nucleic acid
(C) STRANDEDNESS: single
(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: cDNA

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 7:

AGAACCGCGA CCTCCGCAAC CTTGAGCGGC ATCCGTGGAG TGCGCCTGCA GCTACGACCG 60

CAGCAGGAAA GCGCCGCCGG CCAGGCCCAG CTGTGGCCGG ACAGGGACTG GAAGAGAGGA 120

CGCGGTCGAG TAGGTGTGCA CCAGCCCTGG CAACGAGAGC GTCTACCCCG AACTCTGCTG 180

GCCTTGAGGT GGGGAAGCCG GGGAGGGCAG TTGAGGACCC CGCGGAGGCG CGTGACTGGT 240

TGAGCGGGCA GGCCAGCCTC CGAGCCGGGT GGACACAGGT TTTAAAACAT GAATCCTACA 300

CTCATCCTTG CTGCCTTTTG CCTGGGAATT GCCTCAGCTA CTCTAACATT TGATCACAGT 360

TTAGAGGCAC AGTGGACCAA GTGGAAGGCG ATGCACAACA GATTATACGG CATGAATGAA 420

GAAGGATGGA GGAGAGCAGT GTGGGAGAAG AACATGAAGA TGATTGAACT GCACAATCAG 480

GAATACAGGG AAGGGAAACA CAGCTTCACA ATGGCCATGA ACGCCTTTGG AGACATGACC 540

AGTGAAGAAT TCAGGCAGGT GATGAATGGC TTTCAAAACC GTAAGCCCAG GAAGGGGAAA 600

GTGTTCCAGG AACCTCTGTT TTATGAGGCC CCCAGATCTG TGGATTGGAG AGAGAAAGGC 660

TACGTGACTC CTGTGAAGAA TCAGGGTCAG TGTGGTTCTT GTTGGGCTTT TAGTGCTACT 720

GGTGCTCTTG AAGGACAGAT GTTCCGGAAA ACTGGGAGGC TTATCTCACT GAGTGAGCAG 780

AATCTGGTAG ACTGCTCTGG GCCTCAAGGC AATGAAGGCT GCAATGGTGG CCTAATGGAT 840

TATGCTTTCC AGTATGTTCA GGATAATGGA GGCCTGGACT CTGAGGAATC CTATCCATAT 900

GAGGCAACAG AAGAATCCTG TAAGTACAAT CCCAAGTATT CTGTTGCTAA TGACACCGGC 960

TTTGTGGACA TCCCTAAGCA GGAGAAGGCC CTGATGAAGG CAGTTGCAAC TGTGGGGCCC 1020

ATTTCTGTTG CTATTGATGC AGGTCATGAG TCCTTCCTGT TCTATAAAGA AGGCATTTAT 1080

TTTGAGCCAG ACTGTAGCAG TGAAGACATG GATCATGGTG TGCTGGTGGT TGGCTACGGA 1140

TTTGAAAGCA CAGAATCAGA TAACAATAAA TATTGGCTGG TGAAGAACAG CTGGGGTGAA 1200

GAATGGGGCA TGGGTGGCTA CGTAAAGATG GCCAAAGACC GGAGAAACCA TTGTGGAATT 1260

GCCTCAGCAG CCAGCTACCC CACTGTGTGA GCTGGTGGAC GGTGATGAGG AAGGACTTGA 1320

CTGGGGATGG CGCATGCATG GGAGGAATTC ATCTTCAGTC TACCAGCCCC CGCTGTGTCG 1380

GATACACACT CGAATCATTG AAGATCCGAG TGTGATTTGA ATTCTGTGAT ATTTTCACAC 1440

TGGTAAATGT TACCTCTATT TTAATTACTG CTATAAATAG GTTTATATTA TTGATTCACT 1500

TACTGACTTT GCATTTTCGT TTTTAAAAGG ATGTATAAAT TTTTACCTGT TTAAATAAAA 1560

TTTAATTTCA AATGT 1575

(2) INFORMATION FOR SEQ ID NO: 8:

(i) SEQUENCE CHARACTERISTICS:

(A) LENGTH: 333 amino acids

(B) TYPE: amino acid

(C) STRANDEDNESS: single

(D) TOPOLOGY: linear

(ii) MOLECULE TYPE: protein

(xi) SEQUENCE DESCRIPTION: SEQ ID NO: 8:

Met Asn Pro Thr Leu Ile Leu Ala Ala Phe Cys Leu Gly Ile Ala Ser
1 5 10 15

Ala Thr Leu Thr Phe Asp His Ser Leu Glu Ala Gln Trp Thr Lys Trp
20 25 30

Lys Ala Met His Asn Arg Leu Tyr Gly Met Asn Glu Glu Gly Trp Arg
35 40 45

Arg Ala Val Trp Glu Lys Asn Met Lys Met Ile Glu Leu His Asn Gln
50 55 60

Glu Tyr Arg Glu Gly Lys His Ser Phe Thr Met Ala Met Asn Ala Phe
65 70 75 80

Gly Asp Met Thr Ser Glu Glu Phe Arg Gln Val Met Asn Gly Phe Gln
85 90 95

Asn Arg Lys Pro Arg Lys Gly Lys Val Phe Gln Glu Pro Leu Phe Tyr
100 105 110

Glu Ala Pro Arg Ser Val Asp Trp Arg Glu Lys Gly Tyr Val Thr Pro
115 120 125

Val Lys Asn Gln Gly Gln Cys Gly Ser Cys Trp Ala Phe Ser Ala Thr
130 135 140

Gly Ala Leu Glu Gly Gln Met Phe Arg Lys Thr Gly Arg Leu Ile Ser
145 150 155 160

Leu Ser Glu Gln Asn Leu Val Asp Cys Ser Gly Pro Gln Gly Asn Glu
165 170 175

Gly Cys Asn Gly Gly Leu Met Asp Tyr Ala Phe Gln Tyr Val Gln Asp
180 185 190

Asn Gly Gly Leu Asp Ser Glu Glu Ser Tyr Pro Tyr Glu Ala Thr Glu
195 200 205

Glu Ser Cys Lys Tyr Asn Pro Lys Tyr Ser Val Ala Asn Asp Thr Gly

210 215 220

Phe Val Asp Ile Pro Lys Gln Glu Lys Ala Leu Met Lys Ala Val Ala
225 230 235 240

Thr Val Gly Pro Ile Ser Val Ala Ile Asp Ala Gly His Glu Ser Phe
245 250 255

Leu Phe Tyr Lys Glu Gly Ile Tyr Phe Glu Pro Asp Cys Ser Ser Glu
260 265 270

Asp Met Asp His Gly Val Leu Val Val Gly Tyr Gly Phe Glu Ser Thr
275 280 285

Glu Ser Asp Asn Asn Lys Tyr Trp Leu Val Lys Asn Ser Trp Gly Glu
290 295 300

Glu Trp Gly Met Gly Gly Tyr Val Lys Met Ala Lys Asp Arg Arg Asn
305 310 315 320

His Cys Gly Ile Ala Ser Ala Ala Ser Tyr Pro Thr Val
325 330

## CLAIMS

1. Cathepsin L at a specific activity of at least 40,000 nmoles/min/mg.

2. Cathepsin L at a specific activity of at least 100,000 nmoles/min/mg.

3. Cathepsin L in crystalline form.

4. Cathepsin L according to claim 3 in which the crystals possess a monoclinic space group $P2_1$, with unit cell dimensions $a$ = 46.23, $b$ = 49.38, $c$ = 49.25 Å and $\beta$ = 113.45°.

5. Cathepsin L according to claim 4 in which the crystals are wedge-shaped crystals having the atomic coordinates set out in Example 4.

6. A secretion vector for directed inducible expression of cathepsin L into the periplasm of *E.coli*.

7. An *E.coli* host comprising a secretion vector for directed inducible expression of cathepsin L into the host periplasm.

8. A method of making cathepsin L which comprises culture of an E.coli host as defined in claim 7 in a growth medium and optionally soluble cathepsin L is collected from the growth medium.

9. A method of making cathepsin L according to claim 8 in which the E.coli host is cultured at a temperature of 15-30°C.

10. A method of making cathepsin L according to claim 8 in which the E.coli host is cultured at a temperature of about 25°C.

11. A method of making cathepsin L according to claim 8 in which the E.coli host is cultured at a temperature of about 25°C in the presence of a concentration of inducer optimised for maximal soluble expression of cathepsin.

12. *E. coli* MSD 2148 (MSD 213 pZen 1677) deposited under NCIMB accession no 40773.

13. The X-ray coordinates of cathepsin L as defined in Example 4.

14. The X-ray coordinates of the active site of cathepsin L as defined in Example 4 in residues 17-26, 29, 61-75, 111-118, 132-145, 158-166, 183-189 & 209-214.

15. A method of rational drug design using a 3-dimensional structure of cathepsin L as determined from X-ray diffraction data which comprises any of the following:

searching real and virtual compound databases for potential drugs; computational growth of potential ligands in the active site; or collecting X-ray diffraction data from crystals comprising potential drug.

16. A novel inhibitor of cathepsin L determined by rational drug design according to the method of claim 15.

EC70116

AFG/MB : 10OCT96

The Patent Office

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**Application No:** GB 9622436.5
**Claims searched:** 1 to 16

**Examiner:** Mr S J Pilling
**Date of search:** 17 February 1997

# Patents Act 1977
# Search Report under Section 17

**Databases searched:**

UK Patent Office collections, including GB, EP, WO & US patent specifications, in:

UK Cl (Ed.O): C3H (HB7E)

Int Cl (Ed.6): C12N 9/64

Other: ONLINE: WPI, DIALOG/BIOTECH

**Documents considered to be relevant:**

| Category | Identity of document and relevant passage | Relevant to claims |
|---|---|---|
| X | Biol. Chem. Hoppe-Seyler, Vol. 376, June 1995, M Dolinar *et al*, "*Expression of full length human procathepsin L cDNA in Escherichia coli and refolding of the expression product*" pages 385 to 388, particularly page 387. | |
| X | Biosci. Biotech. Biochem., Vol. 57, No. 9, 1993, J J Lee *et al* "*Purification and characterization of proteinases identified as cathepsins L and L-like (58 kDa) proteinase from mackerel (Scomber australasicus)*", pages 1470 to 1476, particularly Table 1 on page 1473. | |
| X | Febs Letters, Vol. 336, No. 3, 1993, T Ogrinc *et al*, "*Purification of the complex of Cathepsin l and the MHC class II-associated invariant chain fragment from human kidney*", pages 555 to 559, particularly the results and discussion. | |
| X | Journal of Chromatography, Vol. 568, No. 1, 1991, V Dalet-Fumeron *et al*, "*High performance liquid chromatographic method for the simultaneous purification of cathepsins B, H and L from human liver*", pages 55 to 68, particularly the results. | |
| X | Comp. Biochem. Physiol., Vol. 96B, No. 2, 1990, M Yamashita & S Konagaya, "*Purification and characterization of cathepsin L from the white muscle of Chum salmon, Oncorhynchus keta*", pages 247 to 252, particularly Table 1 on page 248. | |

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|---|---|---|---|
| X | Document indicating lack of novelty or inventive step | A | Document indicating technological background and/or state of the art. |
| Y | Document indicating lack of inventive step if combined with one or more other documents of same category. | P | Document published on or after the declared priority date but before the filing date of this invention. |
| & | Member of the same patent family | E | Patent document published on or after, but with priority date earlier than, the filing date of this application. |

The Patent Office

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**Application No:** GB 9622436.5
**Claims searched:** 1 to 16

**Examiner:** Mr S J Pilling
**Date of search:** 17 February 1997

| Category | Identity of document and relevant passage | Relevant to claims |
|---|---|---|
| X | J. Biochem., Vol 87, No. 4, 1980, (Tokyo) A Okitana *et al*, "*Purification and some properties of a myofibrillar protein-degrading protease cathepsin L, from rabbit skeletal muscle*", pages 1133 to 1143, particularly Table 1 on page 1139. | |

| | | | |
|---|---|---|---|
| X | Document indicating lack of novelty or inventive step | A | Document indicating technological background and/or state of the art. |
| Y | Document indicating lack of inventive step if combined with one or more other documents of same category. | P | Document published on or after the declared priority date but before the filing date of this invention. |
| & | Member of the same patent family | E | Patent document published on or after, but with priority date earlier than, the filing date of this application. |